The Boston Medical and Surgical Journal

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November 29, 1917

The Massachusetts Medical Society.

SECTION OF MEDICINE.

JUNE 12, 1917.

THE METHOD OF ELECTROCARDIOGRAPHY AND THE ELECTROCARDIOGRAM IN HEALTH.

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FROM time immemorial it has been commonly known that the continuance of life depends upon the constant beating of the heart. The vital necessity for action of this organ has always excited the liveliest interest in everything pertaining to its function. Its anatomy was known to the ancients, but the beginnings of accurate knowledge of its function may be fairly said to date from the work of Harvey. During the nineteenth century, the methods of the physiological laboratory applied to study of the circulation resulted in the amassing of facts of fundamental importance, but it has long been realized that disease of the human heart produces modifications of its action such as we are often unable to duplicate by the methods of the laboratory. A better understanding of the clinical disorders of the heart is certain to result in more thorough knowledge of its normal function and more rational treatment of its disorders.

The first clinician who applied the methods of the laboratory persistently and with result to the clinical study of cardiac disorders was James MacKenzie. You all know his work and the effect it has had upon our outlook on diseases of the circulation. Great as are the advantages of being able to study the time relations between aurieles and ventricles by the graphic pulse method, there was still felt the need for more intimate knowledge of the mechanism of the heart.

For many years it has been known to physiologists that every activity of living substance is accompanied by electrical changes, and that study of the electrical phenomena yields information not readily obtained in other ways. To use the electrical method it was necessary to expose the organ under investigation and attach electrodes directly to it. Even after Waller discovered in 1887 that the action current of the human heart was sufficiently strong so that a fraction of it, tapped off from the surface of the body, would operate a delicate instrument, the electrical method of study was not applied to the human heart except by a few men working in laboratories, because of the difficulties of working with the instruments then available and also because these instruments gave results which required complicated correction methods.

In 1903, Einthoven, professor of physiology at Leyden, described a new electrical instrument, his string galvanometer, very sensitive and extremely quick in responding to electrical currents of brief duration. With the advent of this instrument it became possible to apply the method of studying the action current of the heart as a clinical routine. The first publication

of clinical results with this instrument attracted instant attention, not only because of the important nature of the new information, but also because they were obtained by connecting patients at the hospital in Leyden through wires with an instrument in the physiological laboratory over a kilometer away.

Einthoven's instrument is beautiful in its simplicity as well as in its performance. It consists of a powerful electromagnet with a narrow air-gap between the poles. Stretched vertically in this air-gap is a fine wire of extreme lightness. This is usually made by coating a fiber of quartz glass with a thin layer of metal, and the diameter of the wire so made is about one third that of an average human red blood corpuscle. When this wire is traversed by a feeble current a magnetic field is set up around it, and though very feeble, this field reacting against the powerful field of the electromagnet results in a curving of the wire in a direction at right angles to the field of the electromagnet. In order to make this slight motion evident without weighting the wire with any device for magnifying the motion, as is done in most electrical measuring instruments, each pole of the magnet is perforated in the middle, light is admitted through one opening and a microscope inserted in the other magnifies both the wire and its motion. By illuminating the wire with an arc lamp and projecting its magnified shadow on a screen, the movement can be readily seen. If the shadow is projected through a slit in the wall of a tight box containing a moving photographic film, the movements of the shadow can be recorded on the film, which when developed will show a wavy shadow corresponding to successive positions of the shadow of the wire or "string."

To record the human electrocardiogram with such an apparatus it is necessary merely to connect two points on the surface of the body with the ends of the fine wire by means of suitable electrodes. Einthoven found it convenient to use the extremities as points from which to lead off the current, and employed three pairs of leads: right arm to left arm, right arm to left foot and left arm to left foot.

These for brevity he called leads one, two and three. These leads are universally used and designated in this manner.

It should be remarked that, with suitable accessory apparatus, the sensitiveness of the galvanometer is so regulated that any observer can duplicate the results obtained by another upon the same subject even though they do not use the same apparatus.

It is not possible to speak of a normal form of electrocardiogram, as the curves from different normal people differ quite as much as their facial characteristics. However, the curves in health do not depart from a type which is readily recognized. This typical curve shows three main deflections,—a small rounded elevation, followed by a sharp peak, which is again followed by a rounded elevation larger, as a rule, than the first small one. There are also some lesser deflections less constant and of less significance.

On examining the curve in a patient with heart block we can see at once that the first small rounded eminence is caused by the action of the auricles, the sharp peak and the second elevation being both due to the action of the ventricles.

It may further help us to understand the relation of events in this electrical curve to the heart cycle, as we ordinarily understand it, if we look at a record of the electrocardiogram taken simultaneously with a graphic record of the sounds of the heart. You will see that the first small elevation precedes the first heart sound. The sharp peak begins very shortly before the first sound and the second elevation of the ventricular complex ends just as the second sound of the heart is heard. You have, doubtless, already noticed that we have here in a single curve the means of knowing when the action of the auricles begins and when that of the ventricles follows, so that many circulatory phenomena whose nature we can determine by these time relations can be understood at a glance without the necessity of careful measurement and comparison of two curves, as is necessary in the polygraphic method.

The more important service which the method of electrocardiography renders us will be appreciated from consideration of the changes from the typical form which occur in diseases of the heart. This phase of the subject will be discussed by other speakers. In closing I wish to emphasize a single point. The string galvanometer is an instrument of precision and if used with proper care its results are unimpeachable.

Not so, however, with the interpretation. We have still much to learn and are finding that more than one interpretation may be possible for some of the changes seen.

It behooves us therefore to regard this method, beautiful as it is, as merely a link in the diagnostic chain and to secure and weigh every available scrap of evidence before arriving at a conclusion. By so doing we shall increase our knowledge of the circulation and improve the precision of our diagnoses without falling into those pitfalls which await the enthusiast who puts all his faith in a single method and is led to neglect elementary facts which lie easily within his grasp.

THE SIGNIFICANCE OF ARRHYTHMIAS AND SYSTOLIC MURMURS IN RELATION TO CARDIAC EFFICIENCY.

BY HENRY A. CHRISTIAN, M.D., BOSTON.

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JUST at the present time an increased importance attaches to the interpretation of abnormalities in heart sounds and heart rhythm because, in addition to our regular work in diagnosing and treating disease, we are to be called upon to

examine many young men, to determine whether they are likely to be able to undergo the strain and exertion of military duty. Some cardiac abnormalities are thoroughly consistent with vigorous muscular strain and so need not debar from active service. Others are so regularly indicative of cardiac inefficiency, even though the inefficiency at the time may not be in evidence, as to justify exclusion as unfit. Some hearts are incapable of much extra work though sounds and rhythm are essentially normal.

A purely objective physical examination is not a safe guide in every case. Past history and symptoms not infrequently give the decision as to what interpretation should be placed on certain abnormalities.

Of abnormal cardiac sounds murmurs have had most consideration. Diastolic murmurs, whatever their intensity, location, and propagation, deserve great consideration. With almost no exceptions, diastolic murmurs indicate organic lesions of serious import, and finding a definite diastolic murmur alone is sufficient reason for considering an individual as probably unacceptable for a service requiring severe physical strain, continuing over a considerable period of time.

As we encounter diastolic murmurs, with very few exceptions they indicate mitral stenosis or aortic insufficiency or dilatation of the pulmonic ring. Mitral stenosis is practically always indicative of an organic change in the valve, which will progress and which will lead eventually to cardiac insufficiency either from the mechanical narrowing of the valve orifice or from myocardial disturbances or both.

Many of the patients with mitral stenosis eventually develop auricular fibrillation, and as we will see later a large proportion of patients incapacitated by auricular fibrillation before 40 give the physical signs of mitral stenosis and an antecedent history of rheumatism.

Aortic insufficiency is almost without exception the result of organic change in valve cusps or in aortic wall. In young adults the former is usually the result of rheumatism, the latter of syphilis. Both are serious conditions badly handicapping the heart, with eventual hypertrophy, dilatation and myocardial insufficiency. Dilatation of the pulmonic ring causing the Graham-Steele murmur, though it may be transitory, is indicative of serious cardiac disturbance.

As diastolic murmurs are important, conversely systolic murmurs in young adults are unimportant. A safe rule to follow with systolic murmurs in the apex and left basal regions is to place no significance on them unless accompanied by other evidence of cardiac disability. It makes no odds what the quality of the murmur nor whither it is propagated, this rule is to be followed. It is not possible to distinguish a systolic murmur as due to organic valve lesion by harshness of murmur or by its propagation to axilla, etc.; often soft murmurs indicate more serious disturbance than loud. Were it not for the importance of diastolic murmurs, auscultation well might be omitted in examining young adults, for the systolic murmur *in itself* is of no significance.

It is very infrequent with systolic murmurs at the apex or in the left basal region, unaccompanied by a diastolic murmur, to find at autopsy any evidence of chronic endocarditis of the mitral valve. In older people very often the valve edge is thickened, but an actual organic mitral insufficiency without stenosis is a rare lesion and its possibility practically may be excluded from differential diagnosis. The more hearts I observe in life and then see at autopsy, the stronger grows my conviction on this subject. If a heart is not obviously enlarged, or if auricular fibrillation or pulsus alternans do not exist,—and both of these latter are rare in young people,—the chances that a systolic murmur, without a diastolic murmur, is of any import, are but slight. If there is no past history of rheumatism and the patient experiences no definite dyspnea, the murmur is negligible, and here, again, even if it is harsh and loud.

The views just expressed in regard to systolic murmurs are in full accord with those of Thomas Lewis who has large experience in dealing with British soldiers, being in charge of a special hospital for the study of heart conditions in soldiers. Lewis expresses his views as follows:

(a) "Systolic murmurs at base or apex indicate valvular lesions only exceptionally; there is no conformity of opinion as to the character or conduction of systolic murmurs indicating valvular lesion.

(b) "The extent of mitral valve damage which produces a systolic murmur alone is relatively slight; the disease is often limited to the valve, the heart muscle which is the essential part of the organ being wholly undamaged.

(c) "Patients who are invalided on the ground of systolic murmurs *alone* are subsequently found *when tested* to be fit for active service in nearly all instances. A large number of men who present such murmurs are known to have passed the most severe ordeals of active service without accident.

(d) "If a group of patients who present no murmurs and a similar group in whom systolic murmurs exist are tested in respect to their capacity for work or active service, no difference is to be found in the capacity of the two groups."

His conclusion is: "The presence or absence of systolic murmurs is of no value in estimating the soldier's capacity for work. This practical conclusion holds, irrespective of the character, conduction or point of maximal audibility of the murmur in question."

Some abnormalities in the heart sounds are of much significance. If the apex sounds are ticktack in quality, *i. e.*, if the first sound is shortened and sharpened, or if there is a gallop rhythm at the apex, especially if the rate is rapid or easily made rapid by exertion, the probability that this is of serious import is great. If there is a history of breathlessness on exertion, of pre-

cordial pain, or of anginal attacks, the import is greater. Usually with such sounds the heart is definitely enlarged, but I have seen patients with this type of sounds, with angina-like pain, whose heart was not enlarged to percussion, and yet the myocardium was seriously involved as shown by pulsus alternans or definite disturbances in the ventricular complexes as shown by electrocardiograms indicating lesions in the conduction system, probably from interstitial myocarditis.

Like cardiac murmurs, some arrhythmias are serious, some are of slight importance. Sinus arrhythmia, a periodic change in the rate, the change often synchronous with respiration, is of no significance. Occasionally this type of arrhythmia gives a very prominent irregularity to the pulse. Various types of extra systoles or ectopic beats in themselves are of no significance. If there is no other evidence of cardiac disturbance, extra systoles are to be regarded as not constituting an indication of cardiac disability. The occasional to fairly frequent extra systoles, easily recognized as a dropped beat or an irregularly recurring long pause in an otherwise regular rhythm, seems to do no harm at all. When extra systoles become very numerous they indicate cardiac disability, but under these circumstances there are other indications of cardiac disturbance.

In the patient with extra systoles and a history of palpitation it is particularly hard to form a judgment of the actual cardiac condition, for much of the palpitation symptom-complex is of nervous origin. Probably a safe rule to follow is to judge in these patients of their cardiac efficiency by the amount of breathlessness brought on by exertion or from their vital capacity as measured by Dr. Peabody's method.

Paroxysmal tachycardia, though the heart appears normal between attacks, seems to contraindicate acceptance for military and similar duties because the patient is incapacitated during the attack, and the occurrence and duration of the attack cannot be foretold or prevented. Pulsus alternans is a definite contraindication to physical strain as it indicates severe myocardial disturbance.

Of all the irregularities auricular fibrillation and the closely allied auricular flutter are the most serious. Fibrillation can be recognized easily by the total lack of rhythm in the pulse, the absolutely irregular pulse, and the very common deficit between apex beat and pulse rate, so-called pulse deficit. This latter is observed in almost every case when heart rate is 100 or faster.

Dr. Levine recently has collected the data on the cases of auricular fibrillation observed at the Peter Bent Brigham Hospital (Levine: Auricular Fibrillation: Some Clinical Considerations. *Amer. Jour. Med. Sc.*, 1917, cliv, 43). From this study some very important clinical facts have come. In the first place, it is a common condition, being the cause of cardiac breakdown in a large proportion of chronic cardiac cases. In thirty months we had 128 cases in our wards, and as they are often readmitted it is not uncommon to have 1/10 to 1/8 of our ward patients showing this condition. In 110 of the patients fibrillation persisted, in 18, or 14.1%, it was transient. The patients in whom the condition persisted divide themselves pretty sharply into two groups: a younger group, with definite history of rheumatism and signs of a chronic organic lesion of the mitral valve; an older group, with no history of rheumatism and no signs of organic mitral lesion. About 1/3 of the patients could not be placed in these two groups because there was evidence lacking as to one or the other of the criteria, rheumatic history or mitral lesion. In the younger group females predominate, 24 out of 39, and in the older group males are in excess, 23 out of 35. In only two of our patients over 50 with fibrillation was there a history of rheumatism and signs of mitral disease. The average age of the older group was 20 years older than that of the younger. Syphilis seemed to play a minor part in the etiology of patients with auricular fibrillation.

In the older group all patients had systolic murmurs in the apex region but only extremely rarely were there other signs of valve disease. Such murmurs were regarded as due to dilatation of the mitral ring, and our autopsy experience confirms this view. In 261 consecutive autopsies there were 154 on people under 50 years of age and among these 21 hearts showed chronic organic mitral valve lesions, while in 107, on people over 50, only 2 hearts showed organic mitral lesions, emphasizing the infrequency of chronic mitral disease in older people.

Besides the patients included in the number just discussed, we have observed numerous others in the Out-Patient Department who had auricular fibrillation. The striking thing about them is that they show definite signs of cardiac insufficiency or, if not present when the patient is first seen, these signs soon appear. Contrary to this we have seen some patients with transient fibrillation during acute infectious diseases who subsequently seemed to have undamaged hearts. We have observed two patients not included above who complained of frequent attacks of palpitation, who were observed to have transient auricular fibrillation, while between attacks their hearts seemed normal. Both were well developed athletic young men. This occasional type of case should be regarded in the same light as cases of paroxysmal tachycardia. All other patients with fibrillation, except these and those with transient fibrillation during acute infectious disease, should be considered as definitely incapable of undertaking muscular strain without the greatest probability of cardiac breakdown as the result. Fortunately, in young people, except those with mitral stenosis, auricular fibrillation is infrequent.

In individuals, with or without systolic murmurs, increased heart rate is of significance. If the heart is rapid or, after exercise, the increased heart action persists, the probability of cardiac in-

efficiency is very large. Patients who show the signs enumerated above as indicating cardiac insufficiency practically always have a rapid rate or one persisting after exercise. Even in the absence of these signs, a rate over 85 at rest should arouse suspicion as to the cardiac capability of a prospective soldier. The same is true if the heart does not slow promptly after moderate exercise. In some of these patients, though these rate disturbances do not point to cardiac lesions, they indicate hyperthyroidism, incipient tuberculosis and other conditions just as important as the basis for exclusion from military service.

All of what I have said above in regard to symptoms and signs which should be used to exclude from military service, apply as criteria of estimating probable cardiac functioning power in our patients. In concluding I would emphasize the points I have brought out in regard to systolic murmurs. I am inclined to think that it would be a great gain if systolic murmurs at the apex or in the left basal region were regarded as of no significance in themselves and their presence completely ignored except as a suggestion to look closely for some other sign of cardiac insufficiency.

The Basis of Certain Changes in the Electrocardiogram.

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For the purposes of clinical medicine it may be stated as a fact now generally accepted that the electrocardiogram is a valid record. It is valid because it remains unchanged except for distinct cause from a time shortly after birth until death. Constancy of form of the degree implied here refers to the larger phases of the curves, that is to say, to their general outline. Although the general outline may remain unchanged, small quantitative alterations may, nevertheless, appear. These are important in estimating the action of agents employed in physiological experiments, for small changes in the height and width of waves take place spontaneously. Reliance cannot be placed upon deviations of small size from a control curve, unless it has been ascertained that these do not otherwise occur. We have been interested in the effect of certain physical and chemical agents on the electrocardiogram. Among those tried was the inhalation of oxygen for prolonged periods of time. A series of curves, carefully standardized, was made at about five-minute intervals throughout a period of observation lasting one to two hours. These showed alterations amounting to several tenths millivolts, and were at first presumed to represent the influence of oxygen. So far as I know, curves taken so frequently have not before now been obtained for a purpose such as this, so that it is not known whether alterations of the magnitude mentioned occur naturally. To test the point, a second series was made, without giving oxygen, of the same individual for a comparable length of time under otherwise comparable conditions. In this series we obtained variations precisely as great as in the oxygen series. When the electrocardiogram is spoken of, therefore, as a valid record, capable of exact reproduction over long periods of time and unaltered except for cause, changes of the sort now indicated are understood to take place.

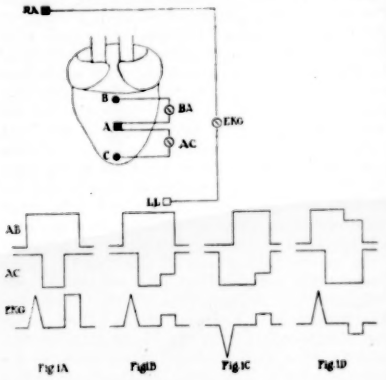
What the electrocardiogram represents has been in general agreed upon. Its waves, of which there are three principal ones, arbitrarily named P, R, and T, recur regularly in each heart cycle. Our principal concern with them until now has consisted in identifying each with an appropriate cardiac activity, so that the P wave is known to be associated with auricular, and the R and T waves to be associated with ventricular activity. Certain activities of the heart have been intensively studied in the light of these electrical curves, and considerable knowledge of the usual size and time or sequence relation of their waves under normal conditions has been accumulated. It is also known what alterations in cardiac mechanism are associated with specified changes in the size and sequence of the waves. By means of this technic, much of what still remained of the subject of the mechanism of irregularities of the heart has been uncovered. Certain groping beginnings have also been made in the direction of understanding what changes have taken place in the form and size and position of the heart, when certain unusual forms of the waves of the electrocardiogram are observed. When waves of a certain type are obtained, such, for instance, in which R_1* is tall and S_3 deep, that is to say, in a curve regarded as showing left ventricular preponderance, we begin to understand what sort of heart has given rise to them. The inference is drawn (1) from a comparison of the electrocardiogram with the roentgenogram, and (2) by analyzing the data so obtained, in the light of post-mortem studies of the weight of the component parts of the heart. Both studies have yielded a degree of knowledge of the meaning of the electrocardiographic waves, but both have revealed difficulties. On the one hand, although roentgenograms of a given type are found in association with electrocardiograms of a given type (the left ventricular type, for instance), similar ones are also found when the electrocardiogram is of a different (the right ventricular) variety. On the other hand, the weights of the various ventricular portions in some cases have not the relation the electrocardiogram led us to expect they would have.

These studies are, of course, based on the hypothesis that the form of the electrocardiogram depends on the distribution of the muscle by

* The small numeral at the foot to the right of the letter indicates the lead (according to Einthoven) employed.

weight in the various portions of the heart, and on the relation of these portions to each other. It is not the purpose of this inquiry to discuss the validity of this hypothesis. I want, instead, to discuss certain experiments which approach the subject of the form of the electrocardiogram from a different point of view, leaving the question open of the relation of the form of the curve to the distribution of muscle by weight.

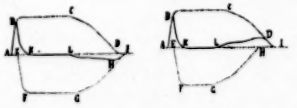
Experiments have been performed by Mines, Boruttau and Samojloff, which show that the electrocardiogram may be regarded as the sum of curves derived in the following manner (Fig. 1). The heart is exposed. A point, A, se-



lected about the center of one ventricle, is then burned so that no electrical potential is formed by the tissue treated in this way. If an electrode is then placed on the base of the ventricle B, and a second one on the neutralized area A, a curve AB is obtained which is monophasic, that is to say, has a single upward deflection, followed by a plateau and ending in a return to the base line. If the electrodes are next placed, one on the same neutral point A, and the second in the region of the apex C, a second monophasic curve AC is obtained, also having a deflection, but this time downward from the base line. The sum of these two curves yields a ventricular electrocardiogram EKG similar to those with which we are familiar. For example, assume (Fig. 1 A) that the first monophasic wave AB described has a value such that the height of the deflection is 9.0 cm., that the deflection maintains this height for 0.4 seconds, and then descends to the base line. And assume that the second monophasic wave AC described has a value such that the depth of its deflection is also 9.0 cm., but that the deflection begins 0.06 seconds after the first, and is maintained for 0.28 seconds only and then returns to the base line. If these two monophasic waves AB and AC are added, it is apparent that an upward deflection will be formed having a height of 9.0 cm. After 0.06 seconds, this deflection will be neutralized by the development of electrical potential in the opposite direction and the curve will return to the base line. But in view of the short duration of the second monophasic wave, its neutralizing power will disappear at the end of 0.28 second, that is to say, 0.34 second after the commencement of the first monophasic one. In view of the fact that this one, the first one, is still active and unopposed, a deflection upward will again appear, in height equal to the first deflection, and will be maintained until the expiration of the potential developed in the first curve. It is immediately apparent that the curve which results in this way from the two added monophasic curves resembles the electrocardiogram. It does not quite resemble the customary curve because of the height of the second or T wave. But the resemblance is made more striking by the introduction of a single complication in the second monophasic curve (Fig. 1 B) in the following way:

The first, or upper, curve is unchanged; the second curve is also unchanged in the first portion. The deflection is maintained for 0.28 second as in the first curve, but then, instead of returning to the base line, it does so only to the extent of 1/3 the distance. Under the circumstances the first, or upper, curve is not unopposed and cannot make its entire influence felt. The second, or lower, curve still having a value of 6, permits it an exercise of potential having the value of 3 only. It is apparent, therefore, that when the small modification introduced in the second figure is considered, the curve resembles more closely the familiar electrocardiogram. There are two chief modifications of the electrocardiogram which are common, the first (Fig. 1 C) a curve in which the R wave is a downward deflection and the second an inverted T wave (Fig. 1 D). The two accompanying diagrams will make clear how the monophasic waves must be arranged in order that such curves may occur.

The diagrams, of course, represent only the principles on which this theory of the formation of the complicated electrocardiogram is based. How the monophasic waves actually appear when a normal curve is analyzed is obtained from the accompanying reproduction of curves taken from Samojloff (Fig. 2). These experi-



ments, then, of Samojloff, Boruttau and Mines are designed to illustrate that theory of the electrocardiogram which supposes these curves to represent the interference of two areas of electrical activity, one developed nearer the base,

the other nearer the apex of the heart, the two probably overlapping somewhat in the intact animal.

Eiger, Lewis, Selenin, and others base their theory of the spiked wave of the electrocardiogram on a system similar to that just described. It differs from it, however, because instead of supposing the curve to result from electrical activity on two sides of a line drawn transversely across the heart, they conceive it to occur on two sides of a line drawn parallel to the long axis and in a sagittal plane, that is to say, the curve results from an interference of the action of the two ventricles.

The important practical bearing of these theoretical considerations is found when the attempt is made to explain alterations in the electrocardiogram, obtained either by experimental or clinical means. They have been observed so far only in the terminal portions of the curve, that is to say, in the T wave or in the interval between R and T. In this portion of the curve a number of agents have been successfully employed in bringing changes about. The agents employed in experiments include the application of heat or cold to one or other portion of the surface of the ventricles, the stimulation of the vagus nerves, or the application of drugs such as muscarin. In clinical medicine it is now known to be caused by the administration of digitalis, and also under conditions which alter the volume of the blood, as has recently been shown by Morison. Of more than passing interest is the relation of the action of digitalis to the form of the terminal part of the curve; indeed, its action may be exerted so that the form of the curve is changed throughout the period from the termination of R to the end of the T wave. The T wave, under its influence, is altered in sign from positive to negative, or from negative to positive.* The alteration occurs in most instances as the first detectable sign of the action of the drug—before changes in auriculo-ventricular conduction occur, and before any sign of the subjective symptoms of intoxication is developed. The sign has, indeed, been found of value in administering the drug, especially in ascertaining the effectiveness of a given preparation and of its sufficient dosage. It is not yet known—though the knowledge is worth possessing—whether the time at which the T wave change occurs represents the point beyond which it is not important to push the drug to obtain a beneficial effect. If it were true that the altered T wave represents such a point, a definite advantage in digitalis therapy would be gained. The belief is now expressed that the point of change in the T wave is the point beyond which pushing the drug represents no advantage.

Theories which consider the factors underlying the formation of the terminal portion of the ventricular curve are few. That the T wave depends on the relation of two monophasic waves such as we have just considered, is, no doubt, plausible. But what the factors are that determine these electrical values is still doubtful. It has been maintained by Lewis and by Cotton, following the initial suggestion of Einthoven, that the relative weight of the muscle of the different portions of the ventricles is the essential determining factor. And while, on the whole, this may be true, we have already seen that the form of the T wave may change frequently and quickly in the same individual under the influence of digitalis and of alterations presumably in blood volume. Under these circumstances an alteration in muscle weight or of muscle volume is out of the question. Emphasis may be placed, in passing, on the fact that under these circumstances the first spiked (R) wave does not change. But other properties of muscle, so far not suggested in this connection, may result in changes in the electrocardiogram. These should be subjected to investigation.

At first it is striking that the portion of the electrocardiogram, which alters under the influences that have been mentioned, is the later part of the ventricular electrocardiographic complex. Apart from other considerations, this should not be surprising because the terminal part of the electrocardiogram refers actually to the greater part of the curve. The initial part of the electrocardiogram is a small portion of the total period of the cycle, because its formation depends, as has been shown, on the initiation of electrical potential in the various parts of the ventricles. This occurs rapidly, but at different instances of time. Why a difference in time occurs, we must attempt to make clear. We are taught as the result of the most recent experiments that the impulse which sets the ventricles into activity reaches all portions of its substance at substantially, but not exactly, the same time. Experiments in dogs, indeed, have shown that there are differences of a little less than three one-hundredths second. Although they are small, these are none the less sufficient to permit an explanation of the spiked wave, on the basis of the pair of monophasic waves that have been described. It is impossible, as yet, to show exactly in what manner in a given heart the time of arrival of the impulse at different sites determines the nature of the interfering electrical responses which serve as the basis of the form of the first or spiked wave, nor to assert that time is the only factor concerned. But it is not difficult to understand certain conditions which can be responsible for alterations in the form of the spike. Normally the form of the spiked wave is probably maintained, first, by the fact that the pathways an impulse must travel, and consequently the length of time required, to reach the various portions of the ventricular muscle, maintain similar relative lengths; and second, that the difficulty or facility of impulse travel over these pathways is equal in the two ventricles. It be-

* Nicolai and Simons reported first an instance of the latter sort. By an oversight, this reference was omitted from our earlier reports.

comes clear that should there arise either an alteration in relative length, as, for instance, in dilatation of the left ventricle, or increased difficulty in impulse passage, in one or more portions, as in toxic heart block or in bundle branch lesions, that the usual balance will be disturbed. What may be expected to follow as the result of such disturbances is an alteration in the relative value in time of the two monophasic waves we have been considering. Should the impulse pathway be altered so that the impulse reaches the second earlier than the first, the inverted spike is the form we should expect.

If the formation and form of the first ventricular waves depend on forces such as have been described, it follows that the actual weight of the muscle which constitutes the walls of the ventricles and enters the septum need not have altered to produce change. But we are not yet in a position finally to adopt this view.

Finally, it may be urged that the fundamental changes in the electrocardiogram have been explained as due to alterations in relative weights on the basis of a crude technic. The theory has been that the muscle which confines each ventricular cavity is an entity. We know, however, from the work of MacCallum and of Mall, that this arrangement does not represent the facts, although for rough purposes it serves in most instances. Therefore an elaboration of the weight theory, rather than the introduction of a new hypothesis, may be required, weight being taken in terms of the layers shown by MacCallum and Mall to exist, rather than weight in terms of the cavities' walls. I have attempted to correlate electrocardiograms with the weights of the layers in such dissections, but on account of the difficulty of the technic have not been able to come to a conclusion of the study.

It appears, then, that the electrocardiogram, usually so constant a physical phenomenon, depends on factors scarcely understood. The form of the curve is explained as depending on the algebraic sum of electrical potentials arising on muscular activity in different portions of the ventricles. These may depend primarily on activity above and below a horizontal line through the heart or to right and left of a vertical one. Both views have been suggested, and these are probably capable of being harmonized. But it is at this point that our difficulties begin. On both sides of either of these lines, what are the factors that determine the value of the potential generated? They may, as we have noticed, be altered by a variety of agents,—by nerve stimulation, by the application of heat and cold and chemicals in experiment, by drugs and means apparently physical in human beings. Are these factors which determine changes, the weight of the muscle, its tension, or its ultimate chemical relations? So far the only investigation attempted relates to muscle weight. Studies in other directions have been suggested, but so far the problem is still open to further study.

ACUTE CARDITIS.

BY FRANK TAYLOR FULTON, M.D., PROVIDENCE, R. I.

IN the consideration of the subject of acute carditis it is my purpose to limit the discussion chiefly to the condition as met with in the course of acute rheumatic fever. Commonly, in referring to an acute infection involving the heart, if there is a friction rub one speaks of acute pericarditis. If, perchance, a murmur and other signs develop, one characterizes the condition as acute endocarditis; but the intimate relation between the pericardium, myocardium, and endocardium is such that there is not likely to be a very active infection of any one of them without, to a certain extent, having involvement of one or both of the others. A consideration of the anatomy and of some of the well-known acute cardiac pathology will further convince us that the heart musculature should receive more attention in acute infection than we have been in the habit of giving it.

As you may know, Aschoff and Tawara,[1] stimulated by the desire to discover the reason for the comparative feebleness of hypertrophied heart muscle, examined a large number of hearts very carefully, the result in the majority of cases being negative. In a certain number of cases of chronic valvular disease supposedly of rheumatic origin, they did discover certain inflammatory changes characterized by the presence of what has been called submiliary myocardial nodules. Coombs[2] has since, in corroboration, given a particularly thorough and detailed account of these nodules and their distribution. They are inflammatory in nature—rather smaller than a miliary tubercle, with a groundwork of fibrin in which are various types of cells, some of them leukocytes, some of them plasma cells, some of them endothelial cells, but most important and characteristic of all, very large multi-nucleated cells, these latter of varying size and shape. There is no absolute regularity of distribution, but they are found more commonly in the perivascular tissue, especially in the walls of the left ventricle, but there is some evidence that the region about the central fibrous body is very liable to be invaded. The muscular part of the interventricular septum and the papillary muscles are only rarely involved, and the auricular muscle almost never. They are in the subpericardial tissues, and are quite likely to be present in the fibrous tissues of the valves, most often mitral, but sometimes the aortic and tricuspid. They are more abundant in valves that have been vascularized and deformed from former inflammatory attacks. The evidence seems to be that they always arise in the connective tissue, that they are of short duration, that they may come in successive groups, and that they may vanish into scar tissue.

The question has continually arisen as to whether these so-called Aschoff bodies are characteristic of rheumatism or whether they are

present in association with other infections. Without entering into the discussion, I may say that the weight of opinion and of evidence is that they do develop only as a result of the infection which we have long known as acute rheumatic fever. They have been found in association with chorea, a point which is brought forward to prove the intimate relationship believed to exist between chorea and rheumatism.

Another result of the work of Aschoff and Tawara was the demonstration in detail of the conducting system of the heart. As you know, the muscle bundle of His has long been recognized as the path for the conduction of the impulse between the auricle and ventricle. Tawara found that the main trunk of this bundle passed along below the membranous portion of the interventricular septum, and that just above the muscular portion of this septum it divided into two branches, one going to the left ventricle and the other to the right. He further found that these main branches subdivide into small branches, and ultimately into minute ramifications which are distributed throughout the inner surfaces of the right and left ventricle, being continuous with the so-called Purkinje net-work. I mention this conducting system in some detail because it is of fundamental importance in understanding some of the damage which may be done by a myocardial infection. You can easily see by referring to the specimen which I now show you how readily an acute infection involving the muscle of the heart might encroach upon the system at some point or points and interfere materially with its action. In fact, Aschoff[3] makes the following statement:

"Now we do find not infrequently, especially in cases of rheumatic myocarditis, actual destruction of the smaller and larger branches of the conducting system, the already described specific rheumatic nodular structures having a special tendency to develop beneath the endocardium and occasionally right in the connective tissue sheaths of the system. Such inflammatory multiplication of cells finally destroy the muscle fibers of the conducting system."

When this inflammatory process is particularly active in the region of the main stem of this bundle, the function of the bundle may be seriously interfered with or, for a time, entirely suspended. Normally there is an appreciable time consumed in the passage of the impulse through the main stem of the bundle. The maximum normal time in the passage is about one-fifth of a second. This is indicated in the difference of time in the contraction of the auricle and the ventricle, and can be very readily measured, either by the polygraph or by the electrocardiograph. Whenever there is an increase in the time interval between the contraction of these two cavities, we know that there is an impairment of the conductivity of the bundle.

Formerly, heart-block was considered chiefly in connection with chronic heart disease. It is now recognized as one of the important complications of an acute inflammatory condition of the heart. It may occur with many of the acute diseases, and in acute rheumatic fever it is not at all uncommon. Its recognition is of prime importance; for, if we detect its presence, we have then direct evidence that the myocardium is involved. It may occur at any time during the course of acute rheumatic fever, and may be the only evidence which can be obtained that the heart is actually attacked, for the toxic effect of the infection may temporarily give rise to much the same cardiac symptoms as though the myocardium were actually invaded. Moreover, it may be the first sign to suggest that the infection is of the rheumatic type. White[4] has only recently reported a case of a boy of 18 who came to the out-patient department, apparently suffering from an acute cold of four days' duration, associated with cough and coryza. At that time he had an irregular heart due to acute heart-block, caused by acute myocardial infection. He subsequently ran a typical course of acute polyarticular rheumatism. The writer has recently observed a case in a young physician, an intern in a hospital, who did his hospital work up to the time of the onset of heart-block. The first symptom which he noted that seemed of any consequence was an irregular heart action, associated with a sense of pressure over the precordium. This was found to be due to partial heart-block. The irregularity persisted for one day only. Electrocardiographic records were taken daily and the conduction time, which was at first double that of normal, returned to normal within a week. Rapid heart action with some cardiac enlargement persisted for a good many weeks. There was at no time any fever. Another case observed by the writer was that of a young man of thirty, who three weeks after an acute tonsillitis was admitted to the hospital almost *in extremis*, with acute cardiac dilatation. His heart action was very rapid, but regular. About two weeks afterwards, he developed an irregular pulse which was demonstrated to be heart-block. The irregularity persisted for about two days only. The conduction time was increased for some time. The exact date of its return to normal was not observed, but it was normal three weeks later. The temperature in this case was 104 on admission. It dropped to normal on the following day and was not above normal again, although the heart-block did not develop until two weeks later. In these two cases the diagnosis of rheumatism is not entirely clear. Considering all the evidence, it is fair to conclude that they were caused by the same infecting agent which is the cause of acute rheumatic fever.

So much for the consideration of the effect

of an acute infection upon the conducting mechanism of the heart. There is, however, still remaining a large amount of the myocardium which may be involved without this infection being manifested by any disturbance of the heart rhythm.

Coombs[5] has written rather extensively on the subject of rheumatism, and divides the cases of rheumatic infection in which there are serious heart complications into four groups. In the first and more important group are those cases in which there is general enlargement of the cardiac area with signs of mitral insufficiency; second, those in which the same signs are present, associated with pericarditis; third, those in which there is associated some evidences of valve deformity, either aortic incompetency or a stenosis of the mitral valve; and, fourth, a group rarely represented, characterized by a malignant endocarditis. His studies had largely to do with children, and of these, about three-quarters of the patients belonged in the first group; that is, those in which there is a marked increase in the area of cardiac dulness, and a well-defined systolic murmur. The evidence, according to him, is that the insufficiency which is present under these circumstances is relative, and is due to the dilatation of the left ventricle; and it is fair to assume that this dilatation is due to the inflammatory reaction in the muscle. It is scarcely conceivable that the small vegetations which are frequently observed at autopsy on mitral valves in such cases can have much, if any, influence upon the formation of such a murmur. In two of Coombs' cases which came to autopsy there was considerable enlargement and dilatation. There was a systolic bruit and a sharp diastolic shock felt over the pulmonic area with the accentuation of the pulmonic second and reduplication of the second sound at the apex. In these, there was not the slightest evidence of endocarditis or pericarditis. Briefly stated, his belief—in which the writer concurs—is that a large percentage of cases have myocarditis without either pericarditis or endocarditis that is *demonstrable*. He believes that the cause of death in rheumatic disease, before the age of sixteen, is more often due to acute inflammation of the myocardium than to anything else, and even above this age, it often plays a very important part.

A word with reference to the late sequelae of an acute cardiac infection. It is a difficult matter to estimate the amount of permanent damage which has been done either to the valves, the heart muscle proper, or to the conducting system. Lewis is of the opinion that an ordinary attack is usually only one of a number of steps which lead to the crippling of the heart, and that it is by oft-repeated damage that the incurable rheumatic hearts are produced. However, there is a good deal of presumptive evidence that, after the valve is once damaged, there is a progressive change which leads gradually in later years to those serious valve deformities and insufficiencies which are so commonly met, although there is no question but that hearts with repeated infections are far more likely to fail rapidly. It is certainly true that a valve can never be returned to normal after having become deformed. It is reasonable that the same opinion should be held with regard to the involvement of the conducting system. This involvement may be in the main stem, in either of the two main branches, or in the smaller branches. It may be transient, lasting but a few days, or it may be permanent; it may be a complete destruction of the bundle, or a slight local inflammatory swelling or edema; it may be recognized with fair certainty, on physical examination, by noting the dropped beats if they occur, and with absolute certainty by polygraphic or electrocardiographic tracings. Generally it is rather transient, but its duration may vary a great deal. If produced by some edematous swelling, it is conceivable that it would last only for a day or two; but if produced by inflammatory infiltration, the condition of the block may last for several weeks; or, at any rate, the facility with which the impulse is conducted may be impaired for a considerable period, and possibly permanently.

In acute rheumatism where there is slight impairment of conduction, if digitalis is given, the degree of impairment is likely to be increased and a serious heart-block may occur. On that account one should always be cautious about the use of digitalis in acute rheumatism.

Most cases of auricular fibrillation fall into one of two main groups: one group includes those occurring in elderly people and such cases are of the cardio-sclerotic type; the other group includes those cases which occur in younger people, usually associated with mitral disease, and usually with a history of rheumatism or chorea.

It is well known that the most striking effect of digitalis in slowing the heart rate has been in cases of auricular fibrillation. It is also well known that digitalis reduces the heart rate in these cases by its action upon the conducting system, reducing its conductivity so that fewer impulses are transmitted to the ventricle. It is further known that the bundle once damaged is distinctly more susceptible to the action of digitalis than is the normal bundle, and it is not at all unlikely that in many cases of rheumatic infection, the conductivity of the bundle is permanently impaired. It has been found to be a general rule, however, that the sclerotic cases are not well controlled by digitalis, but that the cases associated with mitral disease with a history of rheumatism or chorea are particularly susceptible to digitalis. It is quite likely that the efficiency of the drug is to some extent due to the previously existing impairment of the conductivity of the bundle.

It is now generally recognized that in acute rheumatic fever there is usually some primary focus of infection aside from that of the joints or the heart. This may

be in the tonsils, in the teeth, or in some other locality. If that focus persists, it is, of course, important to discover it and, if possible, remove it. Whether it is advisable to do this during an acute febrile attack may be questionable, unless there is a prolonged persistence of the symptoms. Absolute rest in bed is imperative. How long the patient should be kept at absolute rest is often very difficult to decide. It is much better to make the mistake of having too much restraint than of giving too much freedom. I think it is quite certain that the majority of cases are allowed to get up too soon. The patient should be confined to bed until there is every evidence that the heart has returned as nearly as possible to its normal condition. During this time the patient should have plenty of fresh air and should be given a well-regulated diet of sufficient caloric value. In no other condition is judgment and tact more needed than in handling these cases. A patient suffering from acute myocardial infection, well treated, may recover so as to live an active, useful life. If badly treated, however, his whole future may be greatly modified by a seriously crippled heart.

REFERENCES.

[1] British Medical Journal, Oct. 27, 1906.
[2] Journal of Pathology and Bacteriology, April, 1911.
[3] *Ibid.*
[4] Amer. Jour. of Medical Sciences, Oct. 1, 1916.
[5] Quarterly Journal of Medicine, October, 1908.

DISCUSSION.

Dr. Samuel A. Levine, New York: My remarks will be necessarily scattered, touching on a point or two brought out in the papers here.

The first thing that occurs to one is, what has electrocardiography taught the medical profession? I think it may be summarized in the statement that it has given us a clearer conception of the heart mechanism. It has taught us a great deal about the irregularities of the heart. We understand them; how often they occur, their clinical significance, and in many instances we know what the future course of events is apt to be, as a result of a certain arrhythmia. That part of the work is almost complete. But the work that Dr. Cohn has mentioned and Dr. Williams has spoken about is a line that may be very fruitful, namely, changes in the form of the curve. The changes in the form of the curve may give us indications as to what is going on in the heart muscle that we cannot get any other way, because, as is needless to say, the electrocardiogram is a delicate representative of the heart mechanism, of something that is going on in the heart, and may be changed by disease. As we will understand the forces that control the form of the curve more thoroughly, we will understand the aberrations of the heart mechanism, and this will help in an early diagnosis of chronic myocarditis.

The recent work done by Oppenheimer and Rothschild of New York is very suggestive, as they have shown that certain changes in the electrocardiogram are frequently present in chronic myocarditis, *i. e.*, the senile heart. So it seems that changes in the form of the curve may be of increasing significance as time goes on.

Dr. Christian spoke about the importance of the history and symptoms in appraising what a heart is doing, and I just wish to emphasize that point. A systolic murmur with a history of rheumatic fever means a great deal more than a systolic murmur without a history of rheumatic fever. A diastolic murmur, as he said, in civil life is significant. Generally it means organic heart disease. Some French military men have recently found soldiers who have had normal hearts, develop diastolic murmurs in the pulmonary area from the strain of war life, who have not had heart disease, and they attribute it to temporary dilatation of the pulmonary ring. That may be of some importance to those of us who meet soldiers with diastolic murmurs in the pulmonary area and with no other symptoms of heart disease.

Dr. White of the Massachusetts General Hospital has found pulsus alternans with surprising frequency in various heart cases, and we all know that pulsus alternans when present is of very grave prognostic significance. The duration of life, on the average, is from six months to a year. Not infrequently one can detect pulsus alternans while taking the blood pressure. I thought it would be worth while to mention this because we do not all know about taking tracings and we do not all have the means of taking them. While recording the blood pressure as the mercury falls from 180, at 160 only every second beat might come through, that is, the stronger beat of the alternating pulse, and as the mercury falls to 150, the other or weaker beat comes through as well. The difference of 10 millimeters between the strong and the weak beat may become evident in taking the blood pressure and one will be thrown on one's guard as to the presence of alternation in this way. That is particularly true in the cases of angina pectoris, where the main symptom may be pain. I remember a case of that type in a man where the pulsus alternans became evident very readily while taking the blood pressure.

The importance of the increase of the conduction time, that is, so-called P-R interval in electrocardiography, comes out in a series of cases which one might call acute polyserositis. There are quite a few cases of acute rheumatic fever which run a course as follows: First, the synovial membranes of the joints are affected, then the synovial membrane around the heart, and very frequently the pleura as well. One has therefore an acute arthritis, acute pericarditis and acute pleuritis. In fact, if one remembers this symptom-complex, one can frequently tell what has happened and what will happen in some of these cases. You may hear a friction rub over the pericardium; then if you listen below the left scapula, you will find bronchial breathing. Sometimes a few hundred cc. of fluid may be removed from the left pleural cavity. These cases always show a lengthening in the time it takes for the impulse to come from the auricles to the ventricles. Lengthening of the P-R interval is an absolute indication of a toxic process going on in the heart muscle, and that lengthening may persist for two weeks or three weeks after the symptoms of rheumatic fever have disappeared. If one appreciates the significance of this, he can see that such a patient has an acute process of the myocardium and, as Dr. Fulton has emphasized, needs a more careful and more prolonged rest treatment than others

might need. This condition may perhaps be the early cause of conditions that we see, such as adherent pericardium and chronic myocarditis.

Even in the presence of a systolic murmur the diagnosis of mitral endocarditis during acute rheumatic fever is extremely difficult. There has not been sufficient time for mitral stenosis to develop, of course. The systolic murmur may be due to valvular relaxation or it may be due to a real endocarditis. We have no means of telling which it is. We do have a definite means (in the electrocardiograph) of telling whether the myocardium is affected, as has been mentioned above, and this means should be employed wherever possible.

In closing I believe it is well to think of the question of heart disease as divided into two problems, one the problem of acute rheumatic fever and chorea, and the other, the problem of cardiac sclerosis. Practically all hearts, excepting the syphilitic, fall into these two groups. The treatment that we give in all heart cases is merely palliative. We help patients, and good treatment is much more effective than poor treatment, but treatment of the young heart should begin with prevention and proper treatment of rheumatic fever and chorea, and the treatment of the senile heart brings us face to face with the prevention and treatment of all the senile changes that are going on in the kidneys, the heart and the arteries.

DR. HORATIO B. WILLIAMS, New York: I should like to say in regard to Dr. Christian's paper one or two things. I have found that in deciding what to do with people who have murmurs it has been a help to me to think in this way: First, the murmur is of significance only so far as the thing which causes it is producing a disturbance of the circulation. If we see the patient for the first time and he has a murmur, that murmur may be one indication of an active endocarditis and it devolves upon us to find out, if possible, whether that is true before we say anything about the murmur. A very slight murmur of any kind whatever, if it is a sign of active endocarditis, means something serious, possibly, and at any rate means we must exercise caution. If the case is not active endocarditis and we know that the murmur has been present for some time, say for several months, we can judge of the significance of the murmur by the extent of muscular hypertrophy which has been produced, and in advising people what to do I have found it pretty safe to advise them to disregard murmurs which have been present for several months or longer and have not produced an hypertrophy.

It has been shown in my laboratory that a little obstruction of the aorta or pulmonary artery will produce most marked hypertrophy of the corresponding ventricle inside two weeks, so we do not need to wait an unconscionably long time before we will get an hypertrophy with a disturbance of the circulation that is really of considerable magnitude.

In regard to the alternating pulse, I should like to say this: I recognize the seriousness of the true alternating pulse, but I do not believe it is admissible to make a diagnosis of a true pulsus alternans simply from palpation with the finger or from tracings of the radial pulse because I have had cases referred to me in which the tracings showed a strong beat alternating with a small beat, the small beat being placed exactly midway between two large beats. When that case was examined further it was found that the weak beat was merely an extrasystole. Being premature, and a weak beat, it takes longer to get the aortic valve open, and by the time it has been transmitted to the wrist the prematurity has been lost. One can usually distinguish such cases by listening at the apex with the stethoscope.

Fibrillation is a serious handicap to a heart otherwise damaged, but it occurs every once in a while in people in whom we cannot find any other sign of cardiac disease, and those people often do pretty well for a long time. I have in mind a man who was an amateur tennis player. He played an aggressive game of tennis, and one day after playing a very hard game of tennis he thought his heart was going harder than usual and he consulted a physician. It was found that he had auricular fibrillation, and his pulse rate, when quiet, was 130. He seemed to feel perfectly well and fit and was advised to take a little digitalis and go on with his work in the regular way and see what happened. He was a mining engineer and took a position in charge of a big mine where his responsibilities were heavy. On one occasion he went down into the mine and when it was time to go up, the apparatus for raising him out of the mine was out of order. He and another man climbed seven hundred rungs of a ladder vertically upward. The other man fainted on the way up, a man with a perfectly good heart, and he had to hold him on the ladder until the faintness was over and then helped him to get to the top. The engineer himself suffered no embarrassment. I saw him three years after I first examined him and he said he was feeling just as fit as ever. What will ultimately become of him I don't know, but it anything else happens to his heart or if he gets any infectious disease where the heart is put under an undue strain, he would not be as good a risk as a normal man.

In regard to extrasystoles, they can occur as often as once every other beat of the heart in a person otherwise healthy without the subject being conscious of their occurrence or experiencing any embarrassment from it. I have seen a young man who went through college and who is now in charge of a big iron works in China, and has been for several years, who had extrasystoles all the time, every other beat, and he seems to have remained perfectly well and fit. I recall another man who was a chauffeur who could get out and crank up a heavy car in winter when it wouldn't start, and any of you who have tried that know it takes an able-bodied man to do it. He had extrasystoles all the time when he was asleep, but when his attention was distracted in any way they stopped.

I have an impression, based on clinical experience, that young men whose extrasystoles come on only when they are quiet are a good risk, and elderly people whose extrasystoles come on as the result of exercise are a worse risk than they would be if they did not have the extrasystoles. I think one can demonstrate the difference between these two classes of cases quite readily.

DR. HENRY A. CHRISTIAN, Boston: I am the only one who has participated in papers or discussions who is a native, so I would like at first to express my thanks and the thanks of the Section to Dr. Williams, Dr. Cohn and Dr. Levine for coming on from New York and to Dr. Fulton for coming up from Providence and adding so much to the value of our afternoon's program.

I am very glad that Dr. Williams brought out

the points which he did in regard to what I had to say. What I had to say was pretty destructive to a good many of our gods. Dr. Williams destroyed a few more that I hardly dared attack as vigorously as he did.

What he said about the pulsus alternans should be emphasized, that is, the importance of a distinction between what you might call a true pulsus alternans, that is, alternation in the size of the pulse beat, not accompanied by an irregularity in the rhythm of the impulse, and a pseudo-pulsus alternans such as is often found in auricular fibrillation or with recurring extrasystoles. Very often in these you will get an apparent pulsus alternans with variations in the size of the beats, but it has not the same significance as the true pulsus alternans.

Then I think distinctly important is what Dr. Paul White has emphasized in one of his papers, the appearance of true pulsus alternans following ectopic beats; that is, the patient's pulse is quite regular for six, eight or ten beats and there is no alternation of the pulse, then there is an ectopic beat and following that ectopic beat the regular successive beats for three or four beats show a definite alternation. This symptom is an earlier process of what later on becomes a more maintained and more persistent pulsus alternans.

It regard to the elderly people, I did not have that in mind in relation to the extrasystoles because I was talking particularly about the younger people, —of people in whom the question would come up for military service and so on.

The two cases that I referred to of intermittent auricular fibrillation are apparently existent in people who are perfectly normal. They do not have any shortness of breath, no edema, no symptoms at all except palpitation, when they have this auricular fibrillation. One of these fellows is distinctly uncomfortable at the time, and when I have seen him in the attacks I would say at that particular time would be unfit to be sticking another fellow with a bayonet. I think he would get the worst of it if he had an attack at that time. It is more or less like an attack of paroxysmal tachycardia where between attacks the patient is capable of physical strain but during attacks is unfit.

I was very much interested in what Dr. Fulton had to say about acute carditis. I think it is very much more common than we ordinarily regard as being the case, a very considerable per cent. of the cases of rheumatic pericarditis showing disturbance in the conduction time or a definite heart block We were interested in that for a time at the Brigham Hospital and were making electrocardiographic tracings at pretty frequent intervals of patients with acute pericarditis, and distinctly more of those cases than less had a definite disturbance of conduction amounting to a partial heart block. The feature of interest in those cases to us was that it did not seem to make any difference in their immediate prognosis whether they had a heart block or not. They all got well, they all left the hospital with a heart apparently functioning quite normally, and a year or two after that they were all capable of doing a considerable amount of active work; so, notwithstanding the fact they had this definite evidence of lesion in the myocardium, they are not seriously handicapped so far as the immediate future is concerned. Of course very likely in the future,—possibly in eight or ten years or longer,—they might show advanced mitral stenosis and then they might go to pieces sooner with a defective myocardium, probably with auricular fibrillation.

Then finally in regard to the form of the electrocardiogram, which was discussed by Dr. Cohn and touched upon by Dr. Williams—we are very much under obligation to both of these gentlemen for the excellent studies they have been conducting on this phase of the subject. As Dr. Levine pointed out, it is one of apparently very great importance in the consideration of our cardiac cases. The disturbances of the ventricular complex and their relation to muscle disturbances involving the terminations, the minute terminal arborizations of the conduction system, as just hinted at in Dr. Fulton's diagram, are very important. The network of conduction fibres is extremely rich in the heart; there is an interlacing network of those fibrillae everywhere under the endocardium of the ventricles, so that lesions that affect the heart muscle have a very good opportunity to disturb in some way the electrical conductivity of the heart or the electrical impulses, and these disturbances are expressed in changes in the form of the ventricular complex, and we are learning to put much greater importance upon these changes.

It is these experimental studies that are particularly valuable for giving us a clinical basis for the interpretation of these variations in the ventricular complex, and, as Dr. Levine said, it is one of the very important fields now under study from which I think we can expect applications which are going to be very serviceable to those of us who clinically apply to the individual case such knowledge as we can get about his condition from various methods of study in the effort to improve his condition by therapeutic measures.

DR. FRANK T. FULTON, Providence: I am very glad that Dr. Christian said what he did about the frequency with which the myocardium is likely to be involved in the course of acute rheumatism. I did not emphasize that point, but I quite agree with what he said in reference to it Inasmuch as this is the only positive sign available that the myocardium has actually been invaded, it seems to me that it ought to be made a rule, whenever possible, to have careful electrocardiographic observations upon all rheumatic cases. As everyone knows, a case of rheumatism may be very mild, but subsequently show serious heart damage. It is sometimes a difficult matter on physical examination to detect any cardiac involvement, and such cases of rheumatism are very likely to be allowed to get up within a few days and go about their business. If one knew that there was a definite infection of the heart, as might be determined by an electrocardiogram, one would be much more careful about the immediate future of the patient.

TREATMENT OF PERNICIOUS ANEMIA—ESPECIALLY BY TRANSFUSION AND SPLENECTOMY.

BY GEORGE R. MINOT, M.D. BOSTON, AND ROGER I. LEE, M.D., CAMBRIDGE, MASS.

[From the Medical Service of the Massachusetts General Hospital.]

BEFORE taking up the actual treatment of pernicious anemia, it seems desirable from our study

of ninety-six cases* in the past three years, and in view of the present state of the knowledge of this disease, to point out certain things on which treatment depends.

The first essential for the treatment of pernicious anemia is a correct diagnosis. The anemias due to chronic hemorrhage, parasites, sepsis, dysentery, malaria, syphilis, malignant disease, myxedema, etc., at times may be confused with primary pernicious anemia; also idiopathic aplastic anemia and various types of splenic anemia and hemolytic jaundice, more especially the acquired type, are to be differentiated from pernicious anemia. Certain cases of anemia resembling pernicious anemia, associated with pregnancy, with chronic polyarthritis and with grave liver disease, also belong to another class. Quite probably certain cases apparently not hemolytic jaundice with the blood picture of pernicious anemia, but with a hemolytic type of anemia and a very large spleen, had also better be grouped separately from pernicious anemia,[1] and in the future we may quite possibly more completely further separate cases now grouped as pernicious anemia.

Very few cases are diagnosed until the disease has existed for some months. Important points in the diagnosis are: a history of an insidious onset, of remissions, of sore mouth and tongue, and of spinal cord symptoms, and the presence of achlorhydria without evidence of malignancy. The blood picture is, of course, important, but the diagnosis is not to be made upon this alone. The presence of large deeply staining abnormal shaped red cells, together with microcytes, leucopenia, diminution of platelets, and a high color index, etc., are significant. Likewise, evidence of increased erythrocytic destruction is a valuable diagnostic point.

BLOOD DESTRUCTION AND BLOOD FORMATION.

Two features of the disease are the abnormally increased destruction of the erythrocytes and an abnormal type of blood formation. It is evident that at any given time the number of blood elements merely represents the balance of destruction and formation. In judging the prognosis of a given case and the effects and desirability of therapeutic procedures, one should estimate the relative rate and degree of destruction and regeneration of the formed elements of the blood, especially the erythrocytes. This balance of red cell destruction and formation Schneider[2] has referred to as the hemopoietic-hemolytic index.

RED CELL DESTRUCTION.

Red cell destruction can be studied by the excretion of urobilin in the stool[3] or duodenal contents.[4] We have also suggested that it may be studied by the tolerance to intravenous injections of hemoglobin.[5] It is probable that information about erythrocytic destruction can be derived in a simpler manner by the estimation of the bile pigments in the plasma, as determined by the dilution required for the plasma or serum to lose its "yellow" color. We have been and still are studying this, and it has been referred to by Blakenhorn.[6] The degree of icterus exhibited by the patient serves alone as a very satisfactory test, but is sometimes misleading. From the appearance of microcytes in fresh preparations stained with brilliant cresyl blue, one can perhaps derive some information concerning their destruction. The presence of fragmented red cells, as pointed out by Rous and Robertson,[7, 8] are important. The presence of numerous small reticulated red cells we have associated with active regeneration in the presence of increased destruction.

BLOOD FORMATION.

BONE MARROW STIMULATION AND BONE MARROW THRESHOLD.

In order to gauge the power of regeneration and formation of the formed elements of the blood, one must scrutinize the activity of the marrow, not only the intensity but the quality of its activity. Increased activity of the marrow may occur from some stimulus that increases the production of not only one, but particularly of all its three chief elements normally found in the circulation,—the polymorphonuclear neutrophiles, platelets, and red cells. Such increased activity as a method of compensation may be referred to as bone marrow stimulation. The evidence of this can perhaps best be formulated as follows: increases over previous counts in a given patient of the polymorphonuclear neutrophiles, platelets, perhaps particularly if these are of small size, and the reticulated red cells,* especially when that increase means an increase of total reticulation, showing many nodal points in the reticulum, and when all the reticulated cells are not large ones. Decreased activity is associated with an absence or diminution of the factors indicating activity.

Under certain conditions in pernicious anemia this method of marrow compensation is inadequate or cannot be effected. In some instances, as Naegeli[9] has suggested, nature appears to make an effort at compensation by lowering the level of a theoretical barrier that is normally present to prevent all the marrow elements from being poured forth. The result of such an altered threshold is that the more immature elements, that nature tenaciously conserves, enter the circulation. This method of compensation, if persistent or marked, is often to be looked upon as indicating a serious condition, and may often be seen as a terminal picture when the elements of the marrow are poured forth into the blood stream. This lowered threshold is rather espe-

* The diagnosis of idiopathic pernicious anemia was unquestioned. All the cases had complete laboratory studies, nearly all had roentgen-ray examinations of the gastro-intestinal tract.

* Reticulated red cells are young cells, normally about .8% of the red cells. The reticulating is best demonstrated by staining with brilliant crystal blue and is not seen with Wright's stain.

cially evidenced in the erythrocytes as indicated by the presence of many blasts, particularly early forms, and nuclear remains, as Cabot ring bodies, chromatin particles and Howell-Jolly bodies. The presence of these latter structures in the peripheral blood is especially associated with altered splenic function, and especially after its removal. It seems that this organ has in some manner a regulatory action over the marrow. When Howell-Jolly bodies are present, they do not necessarily vary with the presence of even many blasts. With the presence of many blasts, there is inevitably associated an increase of the reticulated cells, but proportionate to the number of blasts and not as seen with stimulation out of all proportion to their number. Evidence of altered threshold is, perhaps, seen in the white cells by the presence in the peripheral blood of myelocytes, and also large mononuclear cells, often atypical, that give the oxydase reaction, and thus presumably of the myeloblastic series. These may or may not be associated with an increase of the polymorphonuclear neutrophiles. Abnormally large platelets may at times be associated with altered threshold.

It would seem as if different cases of pernicious anemia travelled along with different levels of bone marrow threshold. Exactly how it alters the prognosis and effectiveness of therapeutic procedures is not clear.

From our studies and those of others, it does seem that certain young elements, often taken to indicate stimulation or regeneration of the marrow, do not always indicate stimulation, or at least a favorable sign for the patient.

An apparent difference between an altered threshold and pure stimulation is to be found in the fact that evidence of the former may be seen to develop or increase rapidly, following some procedure, as transfusion or splenectomy, while definite evidence of pure stimulation is not seen for some days, following a stimulative procedure. However, we must realize that we may have all degrees of stimulation and altered threshold occurring at the same time. For example, following splenectomy we see not only stimulation, but what appears to be a favorable and permanent type of altered threshold. With a marked and typical stimulation following transfusion, there occurs within 24 hours a rise in the polymorphonuclear neutrophile count. In about two days the number of platelets begin to rise, and reach their height in 3 to 5 days more, then falling somewhat, but remaining at a higher level than before, as do the polymorphonuclears. At about the time the platelets begin to rise, or a little later, the reticulated cells begin to rise, and reach their height in 3 to 6 days, and then gradually fall as the necessity for the abnormally rapid bone marrow activity ceases. In some instances there occurs a diminution in the reticulated cells before they begin to rise. A similar marrow reaction is to be seen after the stimulus caused by direct hemorrhage in man and recently studied in dogs by Drinker.[10]

An unusual, though clear cut, example of altered threshold was seen in a case that chronically exhibited 5 to 8% of blasts, with few polymorphonuclears and platelets which, following transfusion, exhibited within a few hours about 40% of blasts and no particular rise in the other bone marrow elements. Similar less striking instances were seen after exercise in this patient, as has been observed in dogs by Drinker.[10]

Cases that improve rapidly are the ones that show the picture of marked stimulation, though it should not be lost sight of that a similar picture may occur in the presence of excessive red cell destruction, but owing to this destruction the red count does not rise. The cases that improve more slowly usually maintain with the rising hemoglobin and red count a higher polymorphonuclear and platelet count. In such cases the rate of the rising count does not demand any special excess of young red cells,—the reticulated cells,—so that they do not appear in particularly increased numbers. Some cases with lessening of the erythrocytic destruction, or by a very slowly reacting marrow may, perhaps, become slightly improved without particular alteration of the output of the bone marrow factors. However, the higher the polymorphonuclear count, not associated with complications, and the higher the platelets, the better is the regenerative power of the marrow. These two factors are especially valuable in judging the regenerative or reserve power of the marrow in pernicious anemia. The platelets are particularly significant, and seem to be the best single indicator of the activity of the marrow in this disease, for no marked improvement occurs unless they show a definite increase. The other elements may increase considerably and the platelets slightly or not at all, but then only a mild or slight improvement occurs.

Some cases showing inactivity of the marrow may later have good remissions with increased activity of the marrow. Hence a temporary depression of the marrow is not as bad a sign as a permanent depression.

It is the level of the hemoglobin rather than the red count that coincides with the well-being of the patient. It is somewhat obscure how the pigment metabolism proceeds, but in studying hemopoietic activity it is important to observe the relation of the hemoglobin to the red count and young red cells. It would appear as if lower color indices were associated with greater compensating activity of the marrow.

TYPES OF THE DISEASE.

The effect of therapeutic procedures will depend on the duration and type of the disease, and these in turn depend upon the degree of

reserve power of the marrow and the degree of erythrocytic destruction. Judgment about the results of therapy are difficult on account of the natural tendency for remission in the disease. We cannot expect to see and do not see favorable results in cases exhibiting signs of exhaustion or marked depression of the marrow. Cases with marked pouring out of all the marrow elements, likewise, usually die shortly. We also are inclined to believe that cases that chronically exhibit more than a few blasts, associated with an altered bone marrow threshold, usually do poorly, excepting certain splenectomized cases.

It is noteworthy that those types of pernicious anemia that do well spontaneously are the ones that are usually the most favorably affected by therapeutic procedures. The following types of the disease, that merge one into the other, can be recognized.

1. Cases of an acute nature, that rapidly progress to a fatal termination in a few months —the degree of blood destruction varying.

2. Cases with marked or fair remissions, and usually with considerable or marked hemolysis, the hemolysis being greater in relapses, and sometimes not abnormal in remissions. The remissions may be quite sharp or gradual, one or even fifteen in number.

3. Cases that show chronically a considerable degree of hemolysis, with relatively slow and usually never very striking remissions, but do not have, except after years or terminally, very serious relapses. These usually have enlarged spleens, and are affected more favorably by splenectomy than ever seems to occur spontaneously. These cases appear to approach the condition known as acquired hemolytic jaundice.

4. Cases of a chronic nature that slowly progress downward, though interrupted by mild remissions. This type merges directly into Type 5.

5. Cases of a continuous chronic nature that very slowly progress downward with more usually no, or only very slight remissions associated with little increased red cell destruction and a sluggish inactive marrow.

These two latter groups may be termed myelotoxic in contrast to those of groups 2 and 3 that are more hemolytic with perhaps relatively less bone marrow involvement. The duration of the non-acute cases is usually one to four years, though it may be fifteen years. Those of a more continuous nature usually live fewer years than those of a relapsing type. Cases of type 3 are apt to have a rather long course of the disease.

In general, it is the older patients that belong to the myelotoxic type and the younger that belong to the hemolytic types. For example, no case of the chronic continuous type occurred in 13 patients under 40 years of age; 8 of these were cases that had sharp marked remissions. While of 32 patients over 50, of whom 12 were over 60, but 5 had marked remissions, none of whom were over 60 years of age. Of these 32 cases 14 were of the chronic continuous type, of which 7 were over 60.

It has been our experience that usually cases with both enlargement of the spleen and liver (not due to cirrhosis of the liver, passive congestion, etc., but due to pernicious anemia) had more or better remissions, and were better while they lived, so that they ran a more favorable course of the disease, than those without such enlargement. Such cases are also more apt to be more benefited by splenectomy and in some cases without excessive hemolysis, by transfusion than other cases. This enlargement occurs more usually in the cases showing considerable hemolysis, with which it is associated, and is greater later than earlier in the course of the disease. There were 50 cases showing definitely no enlargement of both the spleen and liver. Fifty per cent. of these never had any marked improvement after the disease began and 18% showed marked gains. On the other hand, 40% of the 20 cases with definite enlargement of particularly the spleen but also the liver showed marked gains, and but 15% showed no significant improvement.

Thus we may note that in general the younger patients are more capable of benefit from increased bone marrow activity and an amelioration of the hemolytic factor.

GENERAL TREATMENT AND USE OF ARSENIC.

There is no known treatment that cures pernicious anemia. Occasionally one finds reports of cures, but such instances apparently represent either very long remissions or incorrect diagnoses. Rest in bed and freedom from mental worry and strain, fresh air and sunlight and good hygiene are important, and to be combined with whatever other treatment one employs as well as a suitable diet and treatment directed towards the achlorhydria, cardiac weakness, etc. Such measures are clearly indicated; they prolong life and aid to bring about a remission. Oral septic foci should be removed. Just how far one should go in removing possible septic foci in the internal organs, as the gall-bladder, appendix, etc., as recommended by Percy,[11] is at present open to question.

The use of arsenic by mouth in various forms, preferably as Fowler's solution, has for some time been the chief special treatment for pernicious anemia, and more recently has been used intramuscularly and intravenously. How arsenic is beneficial, is disputed in the literature. It may act as a protective substance to the red cells against hemolysis,[12] though it does not affect the urobilin output.[13] It also may act as a stimulus to the marrow,[12, 14] though in larger amounts it appears to cause destruction of this tissue. Our observations on bone marrow activity following the administration of arsenic preparations are at present inconclusive. However, arsenic does not seem to cause

any very rapid marked stimulation. Salvarsan may at times cause curious bone marrow reactions, as especially shown by increases of certain large mononuclear cells, as reported by Evans,[15] similar instances of which we have seen. Some consider arsenic,[16] especially salvarsan, or one of its substitutes, a valuable and helpful remedy in this disease; others consider that it has no considerable influence.[17] We are inclined to agree with the latter view from our past and present experience with 15 cases (9 not in this series of 96) treated with 3 to 10 small (.1G.-3G.) doses of salvarsan and numerous cases treated for longer or shorter periods with Fowler's solution, and some with atoxyl and sodium cacodylate. Of course, if syphilis is suspected, salvarsan is indicated. We can see no harm arising from arsenic therapy, and in view of a rather prevalent idea that it is helpful, it may be well to use it combined with other therapy, as we have done in some cases. It should, of course, not be given at a time when one is trying to observe the effects of some other therapeutic procedure.

Cases have been treated by many other different methods with varying success, as by cholesterin, extracts of marrow, glycerine, hemolysins, serums, thyroid extracts, etc., etc. Also procedures to cause increased oxygen want, which stimulates the bone marrow, have been recently used,[18] and may in the future have a definite place in the therapy of this disease.

TREATMENT BY TRANSFUSION AND SPLENECTOMY.

The use of transfusion and splenectomy in the treatment of pernicious anemia is relatively new, but seems, from the experience of others and ourselves, to give rather better and more constant remissions than any other methods of treatment. It is, however, possible to parallel the most marked improvement by transfusion and splenectomy, or by either alone, with a case which has had no treatment. However, cases treated by these measures are more likely to show consistent temporary improvement and be more comfortable while they live than without such treatment. How much life is prolonged by these measures is uncertain, and it is possible that when a large series of statistics is available that actual prolongation of life will be found not to occur, except perhaps in certain very limited groups of cases.

Of the 96 cases of pernicious anemia studied, there are 115 observations that may be used for the study of therapeutic procedures. This is because the effect of two different procedures was observed on 19 cases at a time so remote from each other that there could be no confusion of their effects. Forty cases were treated either by no special therapy or by arsenic in some form, and will be taken to represent "untreated" cases. There are suitable data for study of 46 different cases transfused in one relapse of each case. Seventy transfusions were given, not counting the transfusions associated with or given at any time after splenectomy. Nineteen cases were splenectomized, with one operative death in a case with a red count below 1,000,000. Ten cases were treated by exposure of the spleen to the roentgen rays. Only four of the splenectomized cases can be considered selected cases, and the transfused cases represent distinctly non-selected cases.

There was inside of a few weeks definite improvement beyond a simple filling up with transfused blood in about 50% of the 46 cases that were transfused. Very slight improvement occurred in about 13% more, so that about 63% of the transfused cases showed at least some improvement beyond that due to the volume of transfused blood; while 84% of the 19 splenectomized cases showed definite improvement following the operation. The degree of the improvements following transfusion or splenectomy averaged greater than the improvements in the "untreated" cases. In a time proportionate to that in which the transfused and splenectomized patients showed definite or slight improvement, only about 35 to 40% of the 40 untreated cases showed any improvement at all, though it is to be noted that about 80% of any pernicious anemia cases at some time in their course show some definite improvement. There is no conclusive evidence that the duration of the improvements or clear-cut remissions are any longer in the transfused and splenectomized cases than in the untreated ones. However, there were but 7.5% of the untreated cases that showed such marked and rapid gains in the same period of time (about a month) as 30% of the splenectomized and transfused cases did (18% of the transfused and 46+% of the splenectomized). The untreated cases formed a similar number of the different types of the disease as the splenectomized and transfused cases, except that all four cases of the acute type occurred in the transfused group. It is to be noted that the transfused group contained more unfavorable cases than the untreated group, and that 10 of the transfused cases died within a month, while but 4 of the untreated cases did so.

Such figures are suggestive in regard to the frequency, rate and degree of remissions.

TRANSFUSION.

Transfusions[19-27] for pernicious anemia may be employed in relapses to relieve symptoms, and with the hope to bring about a remission. They may be given either repeatedly every few (3 to 7) days, gradually filling the patient up so as to keep him in a better condition, and thus hope to give the marrow a chance to act more normally, as may be accomplished in a different condition, namely, the aplastic anemia of benzol poisoning, or they may be given one to three times some 7 to 14 days apart, with particularly the idea of inducing a

stimulation of the marrow directly or indirectly, or in some manner turning the factors of altered blood formation and destruction to a favorable balance, so as to inaugurate a remission. Transfusion as such has been shown not to influence the excretion of the blood-derived pigments, though in remissions following transfusion these may become lessened as the hemolysis lessens.

In most instances transfusions bring about immediate symptomatic benefit due to the increased amount of blood in the patient. Such benefit is, however, only temporary, and lasts about as long as the transfused blood is held, unless, of course, a remission of some sort is inaugurated. If the patient is exhibiting an excessive hemolytic activity, the transfused blood is at times apparently rapidly destroyed, so that even no real temporary benefit occurs. The beneficial temporary effect is seen in the patient's general sense of well-being, with improvement of appetite, mental symptoms, and often lessening of fever, etc. With the remissions following transfusion, the improvement in the general condition, gastrointestinal symptoms, etc., though the achlorhydria often still persists, is the same as occurs in spontaneous remissions. Transfusions for only temporary alleviation of symptoms may be repeated as often as considered practicable, and may be used when the patient or friends so desire. The desired result to be seen with transfusion is not so much its temporary filling-up effect, but its inauguration of a remission. We have had our cases transfused with particularly this in view. If there has been no result with one transfusion, we have, when possible, had the procedure repeated 1 to 4 times, usually about 9 days apart, for no result with one transfusion does not mean no result with a second. A different donor has nearly always been used for the same patient for each transfusion. There is to be found in the literature[19, 20] an idea that some donors' blood is more capable of inducing a successful reaction in a given patient than others. We are doubtful whether this is true. No noteworthy effects were seen with a donor having polycythemia.

Of the 46 cases treated by transfusion, 9 showed, following this procedure, evidence of a marked bone marrow stimulation, and made very rapid and marked gains in their general condition, and usually in weight coincident with the rising hemoglobin, red count, polynuclear count and platelets. Two of these cases made similar gains following transfusion in another relapse. These cases were all of a definitely relapsing type of the disease, which they had had from 3 months to 6 years, usually 1 to 3 years. In two it was the first relapse, in one the second, in four the third, and one the tenth. One responded only after two transfusions, the others after one. It may be noted here that 6 out of 12 transfusions in 4 similar but splenectomized cases were followed by rapid, marked remissions.

Twenty cases showed a definite but usually slow gain following the transfusions. There was no definite relation of the results to the duration of the disease. One had had the disease under 6 months, five between 6 months and a year, eight between 1 and 2 years, seven between 2 and 6 years. In these cases there was usually at least an eventual increase of some or all the factors, indicating activity of the marrow. In some there were definite increases of reticulated red cells with or without increases of other bone marrow elements an appropriate number of days after transfusion. In others the blood appeared to become maintained at a slightly better level without calling forth any definite increased numbers of the young red cells, in contrast to what occurs with beginning active rapid regeneration. Temporary increase of the polymorphonuclears alone after transfusion in cases previously showing a relative lymphocytosis is not necessarily indicative of future improvement. The studies on the blood elements, hemoglobin, etc., are in some instances obscure and will not be further discussed.

Five of these 20 cases showed a slow progressive improvement, that eventually became marked, 3 having two transfusions, and 2 one. Four belonged to the definite relapsing type of the disease, and 1 was of the type having mild remissions. It may thus be seen that about 30% of the transfused cases had marked improvement, 9 cases rapidly, 5 slowly.

Of the other 15 cases [these cases received from one to three transfusions], 8 showed a moderate or mild improvement, and 7 but a slight improvement.

Such slight improvements were often rather temporary. By improvement following transfusion, we refer here to the fact that there was at least some clinical improvement and some evidence of blood improvement that was present at a time after transfusion, which was not to be wholly attributed to the volume of transfused blood.

Of the 8 cases showing moderate or mild improvement, 6 belonged to a type having relapses, more usually relatively mild relapses, and 2 to a chronic more or less continuous type. Four of the 7 showing but slight improvement were of a chronic continuous type and 3 of a relapsing type.

Seventeen cases showed no improvement following transfusion, beyond the benefits associated with the temporary increased amounts of blood; 10 had one transfusion only, 3 had two, 2 had three, and 2 had four. Both of those having four died two weeks after the first transfusion, one of whom had in a previous remission a marked improvement following a transfusion in New York. Of these 17 cases, 3 died within five days after the first transfusion, 3 within two weeks, and 4 within about a month.

Of the 6 patients dying within two weeks, all

were very sick patients before transfusion. It is not felt that the transfused blood had anything to do with their death, except in two instances where the transfusion reaction perhaps hastened it. Two of these 6 cases had the disease less than six months, and were apparently of an acute type. Four were of a relapsing type. A great activity of the blood-destroying factors was evident in three. Three showed a terminal alteration of bone marrow threshold, as was especially evidenced by many blasts of all types; two of these three cases also showed a high lymphocytosis.

Two of the four cases dying between two weeks and about a month after their first transfusion, and not sooner than three weeks after their last transfusion, were of an acute type, and one of the type showing numerous, very slight remissions, and one was of the continuous type. Both of these last two patients showed enough evidence of bone marrow exhaustion to have secondary purpura hemorrhagica, which is associated with marked diminution of the platelets.[28]

Four of the eleven cases not dying within a month belonged to the continuous type of the disease and had some evidence of an exhausted marrow. Two died within six months, one was in the same condition at the end of two months, and one is now living a year after splenectomy, which procedure, however, caused very little change in the patient's condition.

Two of the remaining three cases that were not improved had evidence of great activity of the hemolytic processes at the time of the transfusion, so that the transfused blood appeared to be rapidly destroyed. One of these cases was splenectomized later, with definite benefit. Other instances where the transfused blood was apparently rapidly destroyed were seen in some of those cases dying shortly after transfusion and in some of those that improved.

The last case to be accounted for had a continuous downward course for about a year and a half, and two transfusions had no effect, though six months later a marked remission occurred, following the beginning of roentgen ray radiations of the spleen.

It may thus be seen that the cases most apt to receive benefit from transfusion are the same as those most apt to have the best course of the disease without treatment. Patients who have had or may be expected to have definite remissions, though the disease has lasted several years, receive the most benefit. While older patients, and those with a chronic prolonged course, with no or but mild remissions, or those with marrow exhaustion, often fail to respond well, the acute forms are not favorably affected, nor are some cases with excessive hemolysis. Though a remission may, perhaps, be inaugurated by transfusion, its duration and character are apparently not different from that which may be expected at that time in the disease.

The figures given may, perhaps, give an unfavorable aspect of transfusion. However, it is to be noted that there is no other procedure that can be so successfully employed for the immediate relief of symptoms, and that after one transfusion the patient frequently requests another; and that patients, in some instances, can be kept alive, if they so desire, by repeatedly filling them up. Also, some very sick cases have shown remarkable gains following transfusion. It has been our impression that transfusion is often, for the time being, actually life-saving in such patients, though it is to be recognized that similar cases occasionally spontaneously have good remissions.

Transfusion, besides giving temporary symptomatic benefit and at times being temporarily life-saving, may inaugurate a remission, even in cases that appear unlikely to remit. Transfusion may allow at once the patient to rest more comfortably, eat more, sleep more, etc., and, either directly or indirectly, permit increased marrow activity, sometimes rapidly, more usually slowly. It thus seems that an opportunity for transfusion ought to be given every case, provided the expected result in a given case is understood by the patient, and it appears that there are many instances where the procedure seems distinctly desirable and of much benefit.

THE AMOUNT OF BLOOD TO TRANSFUSE AND THE TIME TO TRANSFUSE.

The amount of blood that is the most desirable to transfuse is a question that has not yet been definitely settled. Some have advocated large amounts (1000 to 1500 cc.), while others small amounts (100 to 200 cc.). We have had our cases transfused with usually about 600 cc. We have, however, advised large transfusions, and at times very small ones, and have seen definite benefit with amounts from both 150 and 1500 cc. In cases that have a very low red count and low hemoglobin, it is often necessary to give massive transfusions, because in such instances one must give enough blood to increase the amount in the patient's blood stream, while attempting to initiate a remission. Likewise, when a transfusion is done to check hemorrhage associated with marked diminution of the platelets, it is necessary to transfuse a large enough amount of blood to contain enough platelets to check the hemorrhage.[29]

It is quite possible that large transfusions are in some ways harmful, as suggested by Vogel.[29] They may cause actual marrow depression, which we have seen occur following transfusions and which has been experimentally demonstrated in rabbits by Robertson.[30] Following many transfusions, one often first sees a diminution of the reticulated cells before the rise associated with active stimulation. In three instances we have seen a temporary marrow depression twenty-four hours after a transfusion, and lasting about three days, severe enough to allow a mild purpura hemorrhagica to develop,

though two of these cases later had an excellent remission. The other died within a month. Such a purpuric manifestation is probably different from the more rapidly appearing petechiae that occur as one of the forms of unexplained transfusion reactions.

We are inclined to believe that there is a desirable amount of blood to be transfused in pernicious anemia, and that this amount is small rather than large. On the other hand, some cases can do well with an amount that may be harmful to others. The ideal may be to give small amounts repeatedly and often, and at a time when the blood elements are not extremely low, though repeated transfusions may develop some type of substance in the patient's body that makes further transfusions dangerous. Such a method is also often impractical, so that if but one, or possibly two, transfusions can be given, 450 to 700 cc. is recommended. This is the amount that can usually be taken from the donor without causing him any real discomfort, and is enough for the patient to obtain at least symptomatic relief.

In regard to the time to transfuse patients, no set rules can be laid down. It is probably wise not to transfuse if there is a marked blood crisis of some kind taking place. In view of the evidence that anemia *per se* is deteriorating on the various organs of the body, it is desirable to keep the patient above the level of a very marked anemia, and yet not to transfuse when the patient is relatively well. It is certainly wise not to wait until the patient becomes essentially moribund and needs a massive transfusion, though no case is too sick to be able to receive benefit from this procedure. In other words, transfusion is to be preferably done relatively early rather than late. By so doing it is possible that remissions could be more often induced, and by thus letting the patient remain in a relapsed state a shorter time, that life would be prolonged.

CHOICE OF THE DONOR AND TRANSFUSION REACTIONS.

The donor for transfusion should be a healthy individual with a negative Wassermann reaction, and one whose red cells are not agglutinated by the patient's serum, and preferably one whose serum does not agglutinate the patient's cells, so that both donor and patient belong to the same isoagglutination group.[31] A donor should never be used whose cells are agglutinated by the patient's serum, though if this is done it may not always result in an untoward reaction. When the donor is selected by proper, carefully made isoagglutination tests[28-32] there will occur not only no isoagglutination reaction in the patient, but no isohemolytic reaction because isohemolysis does not occur except when isoagglutination does.

In the course of 92 transfusions* in cases of pernicious anemia we have seen three isohemolytic reactions due to improperly made tests.† Further tests showed these all occurred in patients belonging to isoagglutination group IV (Moss), and the donors to group II or III, a combination where the patient's plasma or serum agglutinates, and thus may hemolyze the donor's red cells. This isohemolytic reaction begins while the blood is being transfused. The patient becomes restless, complains of pain in the lumbar region of the back, exhibits altered respiration, and often gastro-intestinal symptoms. Such symptoms are in contrast to the perfect calmness that the recipient should show. Shortly after the first symptoms, the patient has a chill and appears to become toxic as the temperature rises to often 104° F. Later there occurs hemoglobinuria with diminished amounts of urine and often temporarily high blood pressure. Within twelve hours jaundice develops, due to the liberated hemoglobin being changed to bile pigments. The severity of the reaction is over within usually eighteen hours. Most cases that have this reaction get well, while some especially sick cases appear to be unable to overcome the hemoglobin and other toxic products liberated from the red cells.

Isohemolysis probably hastened the death of one of our cases. This was a very sick patient. Another had a slow but marked remission following a second transfusion ten days later, while the third had a rapid and marked remission that began with all the evidences of marked bone marrow stimulation about a week after the unfortunate reaction. There is considerable evidence that products of blood destruction are influential in stimulating the marrow, and perhaps the fact that cases having isohemolytic reactions may receive a marrow stimulation, as others have also reported, further substantiates this view.

Very rarely certain reactions may appear to be of an isohemolytic nature, though the donor is properly selected. Such reactions, however, are due to other causes. Thrombosis is a complication, not a transfusion reaction, that may occur following this procedure.

Besides the isohemolytic reactions which can be avoided by proper tests there are other reactions that occur following transfusion, though usually of a much milder nature. These reactions cannot be foretold and are not ascribed to any special method of transfusion. The cause of these is unknown, though many interesting possibilities have been discussed by Satterlee and Hooker[33] and others. As they suggest, it would seem as if some of these reactions were dependent on the amount of initial coagulation changes that may have taken place in the transfused blood. Novy and DeKruif's[34] recent experiments with anaphylotoxin are significant in

* Most of these transfusions were done by the different house surgeons of the Massachusetts General Hospital. Most of them were given by the Vincent paraffin tube method.

† We did not personally make these three tests.

this connection. We are inclined to believe that the operator who alters the factors of transfused blood the least will experience the fewest reactions, but that such alteration of the blood is not the cause for all these reactions.

In the other 89 transfusions* there were 55 that caused no reaction and 34 that caused some reaction, 20 of which occurred inside of 3 hours and 14 of which were simply delayed temperature elevations. These non-isohemolytic reactions may be briefly summarized as follows:

Eleven consisted of a sharp rise, within an hour, of the patient's temperature of two degrees or more above its previous level, and over 100.5° F., often 104° F., which fell to normal usually within 24 hours and often inside of 12 hours. Three of these cases had a chill.

Four caused very definite jaundice, with at least slight toxic symptoms. A temperature rise of at least 2°F. occurred in 3 cases and a chill in one. These cases had previously received transfusions without any subsequent reaction. They will be referred to later.

Five caused temporarily, within two hours, skin eruptions, 4 urticarial in nature, associated with a rise in temperature in three and a chill in two instances. In the fifth case the skin eruption was petechial in nature and the temperature rose only one degree to 100°F.

Fourteen transfusions caused no immediate reaction, but the patient's temperature began to rise gradually about 6 to 20 hours after the procedure to usually about 101°F., rarely to 105°F. and remained elevated usually 12 to 24 hours and was never accompanied by other symptoms than those of fever. Four of these rises were only a degree and in cases that had not had temperature. Five of these reactions occurred in one case.

Such delayed temperature rises are probably not to be considered of the same nature as the more rapid reactions that follow transfusion, and are often not referred to as transfusion reactions. We have observed perhaps some, but no very definite relation between these different types of transfusion reactions and the condition of the patient. It does seem that some cases are more apt to have certain types of reactions with any donor than other cases.

Only about 6% of the above reactions were severe enough to cause any uneasiness in the minds of those who cared for the cases. One of the reactions probably hastened the death of one very sick patient. The two other similar reactions referred to below, that occurred in extremely sick patients, did not hasten their death. Also none of the other non-isohemolytic reactions caused more than temporary discomfort. The case in which death was hastened received in twelve days 3 transfusions of about 400 cc. each. Following the first two there was no reaction, while following the third, from the same donor as was used for the first, the patient complained at once, particularly of headache, shortly vomiting occurred, the patient became toxic, the temperature rose, and marked jaundice developed and he died in about 18 hours. No hemoglobinuria occurred. Another sick patient, shortly following a transfusion from a donor whom she had previosuly received blood from without ill effects, developed a similar severe reaction. The reaction consisted of a chill, temperature 102.5° F.; gastric symptoms and rapidly marked jaundice developed. Very slight hemoglobinuria occurred. Death occurred two weeks later. A similar, much less severe reaction occurred in a third very sick patient who died 5 days after the fourth transfusion in three weeks.

The isoagglutination tests in these three instances showed no agglutination or hemolysis and we verified them after the reactions in the first two cases. The donors and patients belonged to the same isoagglutination group. Though these reactions may be of some sort of an isohemolytic nature, they are not of the known type. It would seem that they may have been due to the development by previous transfusions of some unknown and unrecognized antibody to the donor's blood. Another, perhaps better, explanation is that the patient's tissues had become saturated with blood pigments due to the red cell destruction during the course of the disease, and the rapid accumulation of pigment from destruction of the previously transfused blood. Hence with further transfusion any pigment liberated by the patient's own hemolytic activity could not be taken care of in a normal manner; consequently the accumulation of such large amounts of pigment in the body allowed a small additional quantity to give rise to toxic symptoms. A similar small amount normally could not do so. The observations referred to below tend to support, but do not wholly explain such a hypothesis.

The case of pernicious anemia that Sellards and Minot refer to in their paper, "The Preparation of Hemoglobin for Clinical Investigations," in this month's *Journal of Medical Research*, is the same one that died in 18 hours after the third transfusion in 12 days. This case showed a greatly lowered tolerance for hemoglobin, similarly as many other cases of pernicious anemia.[5] Following an intravenous injection of 17 cc. of hemoglobin marked toxic symptoms occurred and an intense hemoglobinuria, while two control cases received 20 cc. of hemoglobin and no toxic symptoms or hemoglobinuria occurred.

If we exclude the four slight and delayed temperature rises following these 89 transfusions in pernicious anemia, it is to be noted that these non-isohemolytic reactions occurred in about one third of the instances, a figure close to that given by McClure and Dunn.[24]

Others[19 22 25] give smaller figures (9% to 20%) for the occurrence of transfusion reactions, but apparently do not count delayed tem-

* The isoagglutination tests were all properly performed. Usually they were done by the house officers of the Massachusetts General Hospital.

perature reactions. Not counting the delayed temperature reactions in our cases, there were 22% of the transfusions that caused immediate reactions. It is possible that more of these reactions occur in primary blood diseases than in other conditions.

SPLENECTOMY.

a. Its Effect. Splenectomy for pernicious anemia is a therapeutic procedure that has received considerable attention in the past four years. Giffin,[27] Krumbhaar,[28] Perey,[11] Roblee,[37] Lee, Minot and Vincent, [38 39] among others, and the authorities they quote have reported upon this procedure. Our experience is very similar to that of others and is based on 19 cases,* 15 of which have been reported. The results from splenectomy have not been as great as was first expected and in no way to be compared to the great benefit derived from this procedure in hemolytic jaundice. However, definite improvement follows splenectomy more consistently and uniformly than after any other form of treatment in pernicious anemia. The patients often show marked remissions with red counts over 4,000,000. Splenectomy is in no sense curative, though a more profound change in the blood occurs after splenectomy than by other means. The eventual progress of the disease is not essentially changed by splenectomy, except perhaps in certain younger cases, exhibiting, chronically, considerable hemolysis and enlarged spleens. Whether splenectomized patients live longer, or during the course of their life have more relapses and remissions, cannot be told at present, though it seems rather clear that in many instances there cannot have been more than a slight prolongation of life.

The effect of this procedure seems to be twofold; it not only reduces the red cell destruction, as clearly evidenced by the various tests, and the appearance of the patient within a very few days, but also brings about, by some unknown mechanism, an increased activity of the marrow. This activity may be interpreted as a favorable type of persistent lowered bone marrow threshold combined with temporary active stimulation. Among other features that may be interpreted as an altered threshold are the rapid and persistent appearance of Howell-Jolly bodies, the frequently rapid appearance of blasts and the ease with which they and other nuclear elements appear in relapses following this procedure. Also the rapid and temporary appearance of large mononuclear cells of bone marrow origin, the constant elevation of the polynuclear count and usually of platelets, at least over previous levels, are significant of this altered threshold; as may be the fact that some of the platelets are usually extremely large. Evidence of active stimulation may be seen in orderly rises and falls, first of the polynuclears, then later of the platelets and reticulated red cells. The platelets may reach even five times their normal numbers. Considerable prognostic information is to be obtained by following the blood picture after splenectomy, which we have previously reported on. Some information is also possibly to be derived from observing the degree of decreased fragility of the red cells to salt solution that occurs after this operation.

Quite rapidly, within days after splenectomy and before the red count or hemoglobin rises, one notices as a rule, barring complications, that the patients look better, feel better, and appear less toxic. In some cases the red count and hemoglobin rise rapidly, while in others these factors may not show a definite rise for 3 to 6 weeks. The gains in the general condition occurring before these factors are increased continue as they increase, and the gain in the patient's weight is often striking, though there may at first occur a temporary loss.

Following splenectomy, about 75% of all reported cases have shown definite improvement for three months, and some improvement has occurred in about another 10%. Continued improvement has been seen for six months in between 65% and 70% of the cases, while the cases that have remitted for over a year are few, probably between 10% and 20%. If one considered only selected cases, these figures would be higher.

The operative mortality of reported cases is about 15%, but of the more recent and selected cases it is certainly much lower, about 3% to 5%.

b. Selection of Case for Splenectomy. When splenectomy for pernicious anemia was first done the cases were unselected. The trend now seems to be for a selection of cases, and it is probable that in the future fewer will have their spleens removed. There should be not only selection of the type of case but also selection in the stage of the disease when the operation had best be done.

The following considerations are perhaps helpful in deciding whether to advise splenectomy or not.

It is not indicated in those cases that have evidence of an aplastic marrow or a much exhausted marrow. Likewise it seems that cases, especially with little hemolytic activity, which chronically exhibit signs of a definite altered threshold of the marrow, as particularly told by the continued presence of numerous blasts without alteration in the red count, are not benefited by splenectomy. In many instances older patients and those whose general condition is poor are not desirable cases for splenectomy. Acute cases are a probable contraindication for the operation. Cases that have developed definite spinal cord changes as a rule do not do well with splenectomy, and it is thus not indicated in such cases. Neither splenectomy nor transfusion checks these changes, though some benefit in the symptoms from them may be seen with a rising red count from any cause.

* We are indebted to Dr. Beth Vincent, who did fourteen of these operations, and to Dr. C. A. Porter, who did five.

The cases that usually do well with splenectomy are those of the more hemolytic types of the disease, especially those with enlarged spleens, occurring more often in the younger than the older patients. The rarer cases, exhibiting, more or less chronically, considerable blood destruction and fairly active marrow, with no increased fragility of the red cells to salt solutions, appear to derive more benefit from splenectomy than occurs spontaneously in this type of case. These cases approach the condition of acquired hemolytic jaundice in which splenectomy is usually markedly beneficial. In the future it is quite possible that such cases will be considered a different condition than the more myelotoxic and less hemolytic types of pernicious anemia, usually occurring in older individuals. In this latter type splenectomy is apparently not as effective, though may be followed by striking remissions.

It appears that cases with the larger spleens and secondarily enlarged livers offer good prospects of benefit from splenectomy. Enlargement of these organs in this condition is associated with increased red cell destruction, so that marked icteric discoloration of the skin without bile in the urine will indicate that especially the spleen is responsible for the blood destruction. Its removal will thus diminish the excessive hemolysis at the same time that it inaugurates increased activity of the marrow.

Some true improvement with transfusion is nearly always an indication that there will be rather more improvement with splenectomy because it induces the strongest desirable marrow changes, while no improvement with transfusion may, but by no means always does, indicate that there will be no marked improvement with splenectomy. Thus better results are usually to be seen with splenectomy in the types of cases that do the best spontaneously. Perhaps the more chronic hemolytic types do better with, than without, splenectomy.

The risk of operation is greater when the hemoglobin is below about 30% and the red count about 1,500,000. Such cases should preferably not be operated upon until they have first been transfused, so as not only to increase these factors but also to improve the patient's general condition. Such preoperative transfusions should be given some days before splenectomy, so that one may observe how the patient responds to such a procedure, and also because there are instances where a combination of transfusion and splenectomy at near to the same time have caused a greater reaction in the patient than was to be expected from either alone. In some instances it is necessary to transfuse at a time closely approximating that of the operation, on account of the patient's hemolytic activity or his condition following the operation.

c. *Time to do the Operation.* Splenectomy should preferably not be done during a rather rapid down wave of the disease or in a severe relapse. It also had better not be done at a time when there is evidence of any type of blood crisis, for some fatalities have occurred associated with these. The operation is most satisfactorily done when the course of the disease is stationary or the patient is gradually improving.

If the procedure is to be looked upon as simply the best means of inducing a remission, it then seems logical that it should be used more or less as a last resort when other means have failed. However, splenectomy is not a procedure of desperation and should never be done as an emergency. Unlike transfusion, it can be done but once and does not give rapid symptomatic relief. It should be reserved for selected cases in good operative condition, and in a suitable stage of the disease for operation.

It should always be put very directly to the patient, and if he wishes to obtain the best remission that he can, the operation may be done but not urged. Frequently the operation should probably not even be discussed with the patient on account of his age, and the type and character of his condition, etc. Such a serious procedure should be advised only after considering each case carefully and observing it for some time. It does, however, seem that the operation may be advised, explaining fully the situation to the patient or his friends and, in particular, the younger cases with the larger spleens. There is some reason why, if the procedure is to be undertaken, that it should preferably be done early rather than late. This is because many radical measures are more successful early than late. At present no cases have been splenectomized very early in the disease, a time when pernicious anemia is now seldom diagnosed. Some cases operated upon relatively early may have done better than if not operated upon, even though they have had relapses. It is possible, as Balfour[40] suggests, that if we could remove the spleen in the incipiency of the disease, we might be better able to interrupt the course of the disease and the vicious circle of the hemopoietic system. If the patient is willing to take the risks, there seems no reason why the operation should not be done early. It is perhaps wise in the more chronic hemolytic cases to remove the spleen as early as possible, because, by waiting, at least the anemia acts to cause greater permanent changes in the vital organs of the body, and no permanent harm is known to result from removal of this organ in this disease.

TRANSFUSION AFTER SPLENECTOMY.

Transfusion may be given directly after splenectomy, as McClure has done, so as to keep the patient's hemoglobin and red count as high as possible until he can maintain his own blood at this level. In our cases, as in most others, transfusions in splenectomized cases have been given only in the subsequent relapses.

It has been our impression that relapses following splenectomy have tended to occur rather more rapidly than in non-splenectomized cases,

and also when remissions occurred that they were apt to be relatively rapid. It has also seemed to us, as it has to Vogel,[41] as if splenectomized cases perhaps responded to transfusion better than non-splenectomized patients. We have seen some truly remarkable pictures of very marked bone marrow stimulation following transfusion in our operated cases, so that even 50% of the red cells showed reticulation. If there is eventually any good evidence that transfusion is more effective after removal of the spleen, it would be an argument for early rather than late splenectomy. There is at present no clear evidence that splenectomized cases have more relapses and remissions than untreated cases. When a relapse in a splenectomized case has occurred, one cannot at present say, however, that the disease takes any different course than in many other cases.

Five of our patients have been transfused in relapses following splenectomy. Four cases belonged to a definitely relapsing type of the disease. There were twelve transfusions given these patients in ten relapses. Two transfusions in two patients were without any lasting effect, though another transfusion three weeks later in each case was beneficial. Six transfusions in these four cases were followed by rapid and markedly striking remissions, one by a marked but relatively slow remission and three in one case by a moderately rapid remission but of a relatively slight degree. As is to be seen in any case, untreated or treated, the first remissions were usually longer and better than the later ones.

The fifth case transfused after splenectomy was of a chronic type, who had had the disease ten months with one very slight remission before the operation and who showed an unfavorable blood picture. Splenectomy caused no definite improvement. During the past year, since removal of the spleen, he has had five transfusions, three of which were without more than temporary effect and two were followed by a definite but slight remission.

TREATMENT BY ROENTGEN RAY EXPOSURES OF THE SPLEEN.

In view of the fact that removal of the spleen in cases of pernicious anemia is followed rather consistently by improvement, it seemed that one might be able to obtain some result by exposing the spleen to destructive doses of the roentgen rays. Definite improvement by such treatment has been reported[42] in a few cases of hemolytic jaundice. We have, however, seen no improvement in three cases of hemolytic jaundice that have been so treated. These three cases perhaps serve as a control, because splenectomy is so effectual in the disease hemolytic jaundice, to our ten cases of pernicious anemia treated with the roentgen rays.* These cases have received 6 to 12 treatments with just under the erythema dose of the roentgen rays. The treatments were given two to four weeks apart to a quarter or a half of the spleen.

Two of the pernicious anemia cases are too recent to afford any data. Two showed no improvement and six showed improvement associated with the roentgen-ray treatments. Three showed marked improvement, two moderate and two slight, though all four of those that have gone six months since ending treatment have relapsed. Two cases that showed marked improvement had, before treatments were begun, definite symptoms due to anemia for one and a half to two years, and never had more than very slight remissions. One of these had previously had no remission after one transfusion.

One cannot say that the remissions have been inaugurated by the roentgen rays. What different doses of these rays, radium, etc., applied to the spleen will do towards benefiting the patient remains for the future to tell us. It is possible that some form of radiations to the spleen may be beneficial in this disease.

* Dr. Merrill very kindly gave the roentgen-ray treatments.

SUMMARY.

There is no known treatment that cures pernicious anemia.

From a study of 96 cases and the literature, the treatment of this disease, especially by transfusion and splenectomy, has been considered. Forty of the 96 cases were not transfused or splenectomized.

The first essential for treatment is a correct diagnosis. The diagnosis is not to be made on the blood smear alone and, unfortunately, is seldom made early.

A careful, detailed study of the activity of the bone marrow and red cell destruction is important for prognosis and therapy. Bone marrow stimulation and bone marrow threshold have been discussed. Not only one but all of the three chief elements of the marrow must be studied: the polymorphonuclear neutrophiles, red cells, especially young red cells, and platelets. Observations on the latter are important. Certain elements, often taken to indicate stimulation of the marrow, do not always indicate this, or at least are not always associated with a favorable prognosis. Such elements at times are of bad omen.

It has been pointed out that certain types of pernicious anemia are to be recognized. Those types of cases that do the best spontaneously usually, but not always, receives the most benefit from treatment. Older patients are more apt to have a less relapsing and less hemolytic type of the disease than younger individuals. Cases with enlarged spleens, together with somewhat enlarged livers, when these enlargements are associated with and probably due to hemolytic activity, are apt either to have, or to have had, a more favorable course of the disease than those cases without such enlargements.

It is important that all cases should have proper general treatment.

Transfusion and splenectomy offer the best means for inducing remissions, though a remission can occur spontaneously as marked as those inaugurated by these procedures.

No case is too sick for transfusion. Transfusion can give rapidly symptomatic benefit. It may also, either directly or indirectly, rapidly or slowly, cause stimulation of the marrow or allow increased activity of the marrow, so that a remission is inaugurated.

The amount of blood to be transfused, the time to transfuse, the choice of a donor, and transfusion reactions have been discussed.

Isohemolytic reactions will not occur with properly selected donors. Other reactions of unknown nature, usually much less severe, cannot at present be avoided. It is suggested that some reactions following transfusion may be dependent upon the fact that the patient has previously received transfusions of blood. Such reactions are, perhaps, associated with a rapid and excessive accumulation of blood pigment in the body.

Splenectomy for pernicious anemia is a palliative operation. It checks the red cell destruction and increases the activity of the marrow. Good remissions follow splenectomy more consistently and uniformly than after other forms of treatment. Splenectomy is reserved for only selected cases in certain stages of the disease. It is a serious procedure, is not to be urged, but at times may be advised, provided the patient understands that its effect is only temporary. The cases of pernicious anemia that approach the disease hemolytic jaundice are the most suitable ones for splenectomy.

By means of transfusion and splenectomy we believe that patients do better and can be made more comfortable while they live, and that in certain instances they may perhaps live longer than without such treatment. Probably when transfusions are begun relatively early, so that the patients never remain very anemic for long periods, the best ultimate results will be seen.

Roentgen-ray exposures of the spleen have at present shown no definite beneficial effect.

REFERENCES.

This is not meant to be a complete bibliography of the subject.

1 Moffitt, H. C.: Am. Jour. Med. Sci., 1914, Vol. cxlviii, p. 817.
2 Schneider, J. P.: Journal-Lancet, 1917, Vol. xxxvii, p. 105.
3 Robertson, O. H.: Arch. of Int. Med., 1915, Vol. xv, p. 1072 and references given.
4 Schneider, J. P.: Arch. of Int. Med., 1916, Vol. xvii, p. 32.
5 Sellards, A. W., and Minot, G. R.: Jour. Med. Research, 1916, Vol. xxxiv, p. 469.
6 Blankenhorn, M. A.: Arch. of Int. Med., 1917, Vol. xix, p. 344.
7 Rous, P., and Robertson, O. H.: Jour. of Exp. Med., 1917, Vol. xxv, p. 651.
8 Robertson, O. H., and Rous, P.: Jour. of Exp. Med., 1917, Vol. xxv, p. 665.
9 Naegeli, O.: Blutkrankheiten und Blutdiagnostik, 1912, Leipzig.
10 Drinker, C. K.: In press.
11 Percy, N. M.: Surg., Gyn. and Obst., 1917, Vol. xxiv, p. 533.
12 Block. Thèse de Paris, 1908.
13 Robertson, O. H.: Arch. of Int. Med., 1915, Vol. xvi, p. 499.
14 Stockman, R., and Charteris, F. J.: Jour. of Path. and Bact., 1908, Vol. viii, p. 443.
15 Evans, F. A.: Arch. of Int. Med., 1916, Vol. xvii, p. 1.
16 Bramwell, B.: Brit. Med. Jour., 1909, Vol. i, p. 209; and 1913, Vol. ii, pp. 1093 and 2784.
17 Cabot, R. C.: Modern Medicine, Osler and McCrea, 2d Ed., Vol. iv, 1915, Lea and Febiger.
18 David: Deut. Arch. für klin. Med., 1913, Vol. cixi, p. 2.
19 Ottenberg, R., and Libman, E.: Am. Jour. Med. Sci., 1915, Vol. cl, p. 26.
20 Archibald, A.: St. Paul Med. Jour., 1917, Vol. xix, p. 43.
21 McClure, R. D.: Jour. A. M. A., 1916, Vol. lxvii, p. 793.
22 Larrabee, R. C: BOSTON MEDICAL AND SURGICAL JOURNAL, 1917, Vol. clxxvi, p. 552.
23 Percy, N. M.: Surg., Gyn. and Obst., 1915, Vol. xxi, p. 360.
24 McClure, R. D., and Dunn, G. R.: Bull. of the Johns Hop. Hosp., 1917, Vol. xxviii, p. 99.
25 Brehm, W. V.: Jour. A. M. A., 1916, Vol. lxvii, p. 190.
26 Vogel, K. M., and McCurdy, V. F.: Arch. of Int. Med., 1913, Vol. xii, p. 707.
27 Giffin, H. Z.: Jour. A. M. A., 1917, Vol. lxviii, p. 429.
28 Minot, G. R.: Arch. of Int. Med., 1917, in press.
29 Lee, R. I., and Minot, G. R.: Cleveland Med. Jour., 1917, Vol. xvi, p. 65.
30 Robertson, O. H.: In press.
31 Moss, W. L.: Bull. of the Johns Hop. Hosp., 1910, Vol xxi, pp. 63; and 1911, Vol. xxii, p. 238.
32 Minot, G. R.: BOSTON MEDICAL AND SURGICAL JOURNAL, 1916, Vol. clxxiv, p. 667.
33 Satterlee, H. S., and Hooker, R. S.: Jour. A. M. A., 1916, Vol. lxvi, p. 618.
34 Novy, F. G., and De Kruif, P. H.: Jour. A. M. A., 1917, Vol. lxviii, p. 1524.
35 Lindeman, E.: Jour. A. M. A., 1916, Vol. lxvi, p. 624.
36 Krumbhaar, E. B.: Jour. A. M. A., 1916, Vol. lxvii, p. 723.
37 Robles, W. W.: Jour. A. M. A., 1915, Vol. lxiv, p. 796.
38 Lee, R. I., Minot, G. R., and Vincent, B.: Jour. A. M. A., 1916, Vol. lxvii, p. 719.
39 Minot, G. R.: Bull. of the Johns Hop. Hosp., 1914, Vol. xxv, p. 338.
40 Balfour, P. C.: Jour. A. M. A., 1916, Vol. lxvii, p. 790.
41 Vogel, K. M.: Jour. A. M. A., 1916, Vol. lxvi, p. 1012.
42 Jona, G.: Policlinico, Jan. 9, 1916 (summary in Jour. A. M. A., 1916, Vol. lxvi, p. 696).

DISCUSSION.

DR. BETH VINCENT, Boston: My experience with the methods of treatment in pernicious anemia is confined to transfusion and splenectomy. I should like to speak very briefly of certain points in connection with these two procedures: in the first place, as to the selection of donors for transfusions, and next, in regard to the reactions that one may encounter after transfusion in pernicious anemia. These cases are never such great emergencies but that the compatibility of the bloods of donor and recipient may be determined before transfusion. Not to do so is, I think, almost inexcusable.

The best way to make certain of the compatibility of the blood, the easiest way, certainly, is to determine to which one of the four blood groups the donor and recipient belong. Knowing the blood group, select a donor of the same group as the recipient or, if this is impossible, a donor belonging to Group 4, since it is now very generally agreed that a member of Group 4 is a universal donor and may be safely used with any recipient. Hemolysis sometimes follows the mixture of incompatible bloods. I have never observed a hemolytic reaction between a donor and recipient of the same blood group.

During an ordinary transfusion the patient should be calm and quiet and have a sense of well-being. In a transfusion resulting in hemolysis the signs are usually unmistakable. These signs are immediate and secondary. The immediate signs are observed during the transfusion. The patients complain at once of severe pain in the back or in the abdomen. They have gastro-intestinal disturbances and may vomit on the table. There is dyspnea and a weak, irregular pulse. Under these circumstances one should stop the transfusion at once, no matter how carefully the donor and recipient have been tested. The secondary signs appear within six, twenty-four or forty-eight hours. They are chills, a high fever, the dark urine of hemoglobinuria and jaundice. In most of the cases hemolysis is not

fatal, but if it happens to a very sick patient I think it may add just enough to the burden of that patient to bring about a fatal result. After any transfusion in pernicious anemia there may be a reaction which manifests itself by chills and temperature but which does not interfere with the result. Most of my transfusions have been done by means of the paraffin tube. I have done a few by the citrate method and it seemed to me that a larger percentage of those done with the citrate method were followed by fever and perhaps a chill.

Transfusion does not cure pernicious anemia. It relieves the patient of symptoms due to extreme anemia and may inaugurate a remission of considerable duration. This method of treatment is used in two ways. Transfusions of small amounts of blood are given at frequent intervals to keep the red count at a satisfactory level or a single transfusion of a larger amount—600 cubic centimeters—is made in a relapse when it seems unlikely that the patient will have a spontaneous remission. The latter procedure seems to me the more practical. Each case of pernicious anemia is apt to require several transfusions and, as suitable donors are not always easy to get, it is best to reserve this procedure until needed for the relapses that are sure to come in every case. Except in the terminal stages, a transfusion is not contraindicated by the severity of a relapse. Marked remissions have been observed after transfusions in relapses which threatened to be fatal.

While transfusion is the best treatment for a relapse, splenectomy should not be attempted in this stage of the disease. The remissions following splenectomy are often more marked and sometimes longer than those obtained in any other treatment. The mortality is not high if one does not operate in a relapse. This is the rule at the Massachusetts General Hospital where we have had but one operative death in these cases. If the patients are not in satisfactory condition these cases are transfused from three to ten days before splenectomy. Splenectomy is most clearly indicated in the cases of pernicious anemia in which the bone marrow is active and capable of stimulation, and the destruction of red blood corpuscles is excessive as shown by the patient's yellow color, and the increased urobilin in the stools and duodenal contents. Cases with an enlarged spleen and jaundice form the most hemolytic type of pernicious anemia and resemble the cases of chronic hemolytic jaundice in which removal of the spleen gives excellent results. No matter how responsive the bone marrow, the destructive activity of the spleen is a serious handicap in these cases.

If splenectomy is done in every case of pernicious anemia that presents itself, I am quite sure that the patients will be dissatisfied with the results. These cases should be carefully studied by a medical man and the cases selected for operation according to the indications. A series of cases done under these conditions should give results that will repay the patients for the risk and discomforts of the operation.

DR. R. C. LARRABEE, Boston: I want to say a word in appreciation of the work of Drs. Lee and Minot and their associates at the Massachusetts General Hospital, on pernicious anemia. In the last few years much has been contributed to our knowledge of this common and serious disease, and in this work the authors of the paper have had an important share. Yet in spite of these advances, there are still great gaps in our knowledge of the disease. Interest at present centres about the operation of splenectomy, and most of the recent work had to do with the enormously increased destruction of corpuscles in the spleen and liver. Although this hemolysis is believed to be the primary factor in the disease, we are not justified in saying that pernicious anemia is hyperspleenism in the sense that exophthalmic goitre is hyperthroidism. In the latter condition, thyroidectomy gives permanent relief and we are justified in assuming that the thyroid is primarily at fault. In pernicious anemia, however, removal of the spleen merely produces temporary remission, and does not always do that. Relief is not permanent, and relapse invariably occurs. There is some hemolytic agent or agency at work. We do not know what it is, but it originates or *may* originate outside of the spleen. Splenectomy does not eradicate it, but does remove a wheel in the machinery with which it works. The machinery is sooner or later repaired and the work goes on as before.

In the practical application of splenectomy, we are apt to find ourselves on the horns of a dilemma. On the one hand, though results seem to be about as good when operation is performed late in the disease as when it is performed early, it is not advisable as a last resort, when the patient is failing rapidly. The operative mortality is then high and the chances of benefit small. On the other hand, a palliative operation in a remission is an absurdity—unless it can be proved that the remission will be lengthened and made more perfect, which cannot at present be affirmed. I believe that the operation finds its best field in a rather large group of cases, which are neither in relapse nor remission—patients who drag along in a state of invalidism with the hemoglobin, say, between 40 and 50 per cent. Operation gives a good chance of bringing about a remission without excessive risk.

I have had a small series of transfusions—perhaps a dozen cases—in most of which the patient was losing ground under medical treatment. They fall in three approximately equal groups. In all, the downward course of the anemia has been interrupted by an abrupt upward jog, representing the addition of normal blood. In about a third of them the advance of the anemia has been promptly resumed, so that the benefit has been very brief. In another third the initial improvement has been followed by further progressive gain, and the remissions thus initiated have struck me as being remarkably long and perfect. In the third group the advance of the anemia seems to be checked; the initial gain is more or less perfectly sustained for a short period; but no real remission occurs. These cases may perhaps be favorable ones for splenectomy, which would not have been possible except after the transfusion.

DR. J. B. BLAKE, Boston: I feel I have but little right to discuss this paper; when I was asked to do so, it was from the standpoint of operative experience, and at that time I hoped to have a considerable personal experience. I should like, however, to emphasize two or three points.

I congratulate Dr. Minot on his very excellent presentation of the subject. It should not be forgotten that the suggestion of splenectomy was made not by a surgeon, but by a medical man. That is a matter of some importance. The only other in-

stance I think of in modern medicine was the recommendation of Dr. Reginald H. Fitz, who recommended that all cases of acute appendicitis be subjected to immediate surgical interference.

It is conceivable that splenectomy may take, in the future a larger rôle than it seems to me to occupy at the present time. It is also possible, if every case of pernicious anemia was studied early enough to make a very early diagnosis, that our control over the disease might be greater. We are talking, of course, not of cures but of remissions, and it may be possible that in the small number that are ultimately going to be benefited, a remission may be effected frequently enough to create practically what might be called a cure.

As to the operation itself, I cannot quite accept as general, Dr. Vincent's extraordinarily good figures as applied to mortality in splenectomies. In the Mayo Clinic, where the operation has been done for one thing or another some one hundred and fifty times, the mortality at present approximates ten per cent., and that includes Banti's Complex and other conditions in which the general bodily state of the patient is more favorable than it is in pernicious anemia. I cannot believe that the mortality through the country, as the operation is done by the average surgeon, is much below fifteen per cent. I should think an eventual mortality of five per cent., which is a low mortality for major surgery under conditions of anemia of any sort, would not be reached for some little time.

As to the suggestion made and prominently pushed by one surgeon that not only should the patient have the spleen removed, but also the gall-bladder and appendix, I cannot believe that there is any indication for such a proceeding. The operation for splenectomy is serious enough in itself, and only to be recommended after very careful and continued study by the laboratory expert and the clinician, and the surgeon.

Finally, the question as to the rôle of splenectomy in pernicious anemia is not to be settled by the experience of a single surgeon, or of many surgeons for a single year, but by the results of many surgeons, in many carefully studied cases, over a period of many years. Perhaps ten years from today, we shall know whether splenectomy can cure any case of pernicious anemia, or whether it will help all cases, or whether it is only one method which may help a little to prolong life, but not to preserve it indefinitely.

Dr. George R. Minot: I have noticed this morning in the last issue of the *Journal of the American Medical Association* that Sydenstricker and others at the Johns Hopkins Hospital have reported more striking instances than ours of transfusion reactions that may be due to the development of immune bodies to the donor's blood.

I think that the statistics for the operative mortality of splenectomy in general are higher than those for the operative mortality for splenectomy in pernicious anemia. This may be because in the latter condition the spleens are more easily removed.

Book Reviews.

Eye, Ear, Nose and Throat. A Manual for Students and Practitioners. By Howard Charles Ballenger, M.D., and A. G. Whippern, M.D. New second edition, thoroughly revised. Illustrated with 180 engravings and 8 colored plates. Philadelphia and New York: Lea and Febiger. 1917.

The first edition of this manual was reviewed in the Journal of Dec. 20, 1900, nearly seventeen years ago. It is of the same size as before, but of course has been largely re-written. It covers a wide field in a small space, and is well arranged for reference. It is a posthumous tribute to the value of Dr. Ballenger's contributions to his special field in medicine.

Cerebellar Abscess. By Isidore Friesner, M.D., and Alfred Braun, M.D., F.A.C.S. New York: Paul B. Hoeber. 1916.

This monograph by two New York otologists, deals *in extenso* with the etiology, pathology, diagnosis and treatment of cerebellar abscess, 98% of whose occurrence is otitic in origin. The anatomy and physiology of the cerebellum are briefly outlined as a basis for the neurological knowledge essential to cerebellar diagnosis. The descriptions of the etiology, pathology and symptomatology are based chiefly on the reports of 86 cases collected from the literature since 1906. The work is illustrated with an interesting double page frontispiece showing the cerebellum as described by Vesalius in his "Corporis Humani Fabrica" in 1555, and by eight other full-page plates and sixteen text cuts from original drawings and photographs made by the junior author. The chapter on prognosis and treatment describes and illustrates operative technic. There is an excellent alphabetic bibliography of 106 titles. The book should prove a valuable contribution to the literature of the subject.

A Chart of Food Values. By Paul W. Goldsbury, M.D. New York City: E. C. Bridgman. 1917.

Dr. Goldsbury has devised a chart of food values, showing the principal elements of common foods. Each food is represented by a square, printed in colors to represent the proportions of its component parts. Its caloric value is printed below. There are 48 foods thus portrayed. The information here given in so graphic and simple a manner ought to be common knowledge in every household.

THE BOSTON
Medical and Surgical Journal
Established in 1812
An independently owned Journal of Medicine and Surgery published weekly under the direction of the Editors and an Advisory Committee, by the BOSTON MEDICAL AND SURGICAL JOURNAL SOCIETY, INC.

THURSDAY, NOVEMBER 29, 1917

SUBSCRIPTION TERMS: $5.00 *per year, in advance, postage paid, for the United States.* $6.56 *per year for all foreign countries belonging to the Postal Union.*

An editor will be in the editorial office daily, except Sunday, from twelve to one p.m.

Papers for publication, and all other communications for the Editorial Department, should be addressed to the Editor, 126 Massachusetts Ave., Boston. Notices and other material for the editorial pages must be received not later than noon on the Saturday preceding the date of publication. Orders for reprints must be returned in writing to the printer with the galley proof of papers. The Journal will furnish one hundred reprints free to the author, upon his written request.

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126 Massachusetts Ave., Corner Boylston St., Boston, Massachusetts.

ALLERGIC AND AUTOSEROLOGIC THERAPY.

THERE is, perhaps, no more fascinating field of medicine than that opened by the studies in anaphylaxis—the sensitiveness of the organism to certain foreign agents,—bacteria, toxins, food products or other materials,—especially after repeated contact. It has long been understood that some individuals had an idiosyncrasy for certain foods, substances or poisons. This food sensitiveness or allergy manifests itself in various ways. There are the symptoms of acute poisoning, such as vomiting, abdominal pain, diarrhea, swelling of the lips, tongue, pharynx, and esophagus, besides certain spasmodic effects in the bronchial tubes. The cutaneous eruptions are, perhaps, more striking and suggestive of these symptoms. Urticaria of various forms and degrees and angioneurotic edema are very common accompaniments. Then there are the more chronic skin manifestations, such as eczema, erythema, etc. The chronicity of these skin diseases is due, in all likelihood, to the continued action of these food agents, although the allergic effect is not severe enough at any time to produce the acute symptoms of extreme prostration and collapse. This food sensitiveness seems to depend upon the protein element of the food and sometimes upon the globulin element, particularly the water soluble protein and proteoses. It may be, however, that it is some substance intimately connected with these elements. The anaphylaxis is due either to a lack of some protective element in the body against the action of these protein elements, or to an extreme degree of sensitiveness to them, quite in excess of the protective power of the body. It has been held that this sensitiveness was due to a splitting up of the offending protein into component and toxic elements when in contact with the sensitive organism; and because there is a lack of this protective element which would, under other circumstances, have prevented this untoward splitting. When the offending proteins were in food elements not in the regular dietary, the cause was comparatively easy to discover, and the remedy obvious. But when the offending proteins were included in the regular dietary, and when that dietary was, as it should be, a mixed one, the problem was far more difficult. To separate and to feed each food article separately until the offending one manifested itself by causing symptoms is a method that is tedious and generally impracticable. The method now pursued with food is the same technic as that pursued in the usual anaphylactic methods,—as with tuberculin, for example. A von Pirquet borer is used to abrade the skin, and the food extracts rubbed in one after another, until the one that causes a reaction is reached. The reaction manifests itself by the production, in from 5 to 15 minutes, of an urticarial wheal. Almost any food can be toxic to some individuals. Where they result in persistent skin conditions, which do not yield to treatment or recur, the reactions must be tried out to see whether or not an allergic sensitiveness is at the bottom of it. For testing purposes there have been made commercially various stock food "vaccines." For treatment these substances are put up for internal administration, and given in increasing doses until there is a desensitization. It would seem that desensitization by the skin route would be the more rational method, although the dosage would have to be minute and very carefully planned. However, it must not

be understood that all food toxic effects are due merely to individual sensitiveness, nor that all chronic or repeated skin manifestations are allergic in origin. It must not be understood that the treatment of all skin affections, other than the specific skin lesions, will yield to dietetic or allergic therapy. Proper diet will affect all pathological conditions only as proper diet contributes its share in keeping up the health and in maintaining vital resistance.

More recently many of the obstinate skin diseases have been successfully treated by some observers with autogenous serum. Gottheil, Willock and others report favorable results, while other observers are more skeptical. The most striking results of autoserum treatment have been in the postponement of recurrences, and in the mildness of these recurrences. Whether the principle in this form of treatment is the same as the treatment of hemorrhagic conditions in the new born with foreign sera, is hard to say. Some of the workers have found that better results were obtained, especially in psoriasis, when the autoserum treatment was combined with the usual chrysarobin treatment. The skin condition was cleared up more quickly. The method followed in this treatment is to withdraw about 100 cc. of blood, centrifuge after clotting, and to reinject into the circulation the remaining 25 to 45 cc. of serum.

For the present these two elements in the particular form of toxemia manifesting itself so frequently by skin conditions—that is, allergy and autogenous serum treatment—have come to stay. The mistake will be made in laying all on one or the other theory. Until more is learned on the subject, the most rational method in treatment will be the determination of food idiosyncrasies, and treatment accordingly,—autogenous serum treatment in appropriate cases, and the continuance of the usual but not obsolete methods of treatment heretofore obtaining.

DURATION OF CONTAGION IN SCARLET FEVER.

The colder months of the year usually bring a considerable rise in the morbidity from scarlet fever, and again emphasize the difficult problem of determining cause and effecting prevention. Yet scarlet fever, although serious and having a high mortality, is not nearly as contagious as measles or whooping cough, for example. In the latter the degree of contagion on direct exposure is sometimes as high as 99%, whereas in scarlet fever it is rarely above 37%. The susceptibility to scarlet fever becomes markedly less with the rise in years, and in children is probably at its lowest ebb between 12 and 14 years. Although the specific germ of measles has not been isolated, much work has been done with the virus obtained from the blood. But the specific cause or the specific virus of scarlet fever is still undiscovered. The strains of streptococci and staphylococci found in scarlet fever or associated with the complications do not carry out the postulate for specific organisms. Nor do the so-called scarlet fever bodies found in the skin appear to be more than the products of a severe inflammation. As to the method of contagion, it does seem that here also the disease is spread by contact with the discharges directly from the patient or from objects in contact with them. It is the usual droplet method of infection. Moreover, it is just as likely, although undemonstrated because the specific germ has not yet been isolated, that there is a carrier population which is responsible for the spread of the disease in epidemic proportions. The carrier may be one himself immune to the disease, or having had it in the past in severe or in mild form. Many cases of scarlet fever are undiscovered because they have no constitutional symptoms, but they are just as likely to transmit severe infections as the seriously affected patients. In this disease, more than elsewhere, is the infection likely to be conveyed by objects in contact with the patient, such as toys, clothes, books, etc. Disinfectants do not have much effect on the virus, but heat destroys it, and must be used to destroy discharges from the body or for the sterilization of materials in contact with the patient. In scarlet fever, as in other infectious diseases, the air-borne route of infection, while not disproven, is no longer accepted. Contagion must be effected by means of discharges from the mucous membranes of the nose, mouth and throat, as well as the urine in nephritic complications. As for the desquamatory skin as a bearer of infection, there is still much doubt. In measles, desquamation is no longer held to be a period of contagion. Contagion does not outlast the catarrhal stage, and the scales have nothing to do with the spread of this disease. Rational quarantine does not now outlast the catarrhal stage. In scarlet fever, on

the other hand, there is still considerable hesitancy in absolving the desquamating scales from guilt in the spread of this disease. If there is any contagion, probably the primary desquamation carries more of it than the secondary. The problem that must yet be solved with respect to the desquamation in scarlet fever is whether it is responsible for the return cases. The small number of the return cases and the generally lower degree of contagiousness are not consistent with the long period of desquamation being continually infectious. Perhaps it would be more plausible to say about desquamation that the period of desquamation is an index of the period of contagion, rather than the cause of it. The inflammation which causes the skin eruption and the angina are the same processes. Until there is complete healing, the discharge does not stop, whether it is a discharge of desquamating débris in the skin, or the non-identifiable débris discharged from the mucous membranes. In other words, as long as there is desquamation there is infective discharge from mucous membranes. The healing of the mucous membranes of the nose, mouth and throat may take many weeks, and is the reason for the maintenance of such long quarantines. This quarantine should last in ordinary or in uncomplicated cases from five to six weeks. Until more is known concerning the causation of this disease or the nature of the virus, the actual period of contagion cannot be determined and the quarantine had best be maintained as long as possible.

THE SIGNIFICANCE OF ORAL SEPSIS.

THE progress in dental research and in dental therapeutics has been so marked that this period may well be called the dental epoch in medicine. But the development of this science is too one-sided, in that there is a strong leaning to prosthetic rather than to therapeutic dentistry. There is too much development of mechanical skill and too little scientific conception. Good dentistry must be, first of all, a proper conception of the pathological significance of oral conditions. The presence of decayed teeth, infected gums and diseased bone is not nearly so bad as after the filling or crowning of such areas, because what had previously been an open and perhaps draining wound, is now converted into a closed but, nevertheless infected cavity. This danger in dental work must always be kept in mind if disaster is to be avoided. Although the swallowing of pus from infected teeth may in itself account for the digestive disturbances accompanying oral conditions, this is the very least of the evils of oral sepsis. A great many rather vague medical conditions and more definite evidences of toxemia are directly traceable to oral infection. Mainly, however, one has to deal with definite toxemia the direct result of absorption of bacterial toxins found in the mouth. Most of the vague conditions classed as rheumatic have their inception in the mouth. Acute rheumatic infection, with the endocardiac complications, is either metastatic infection from foci in the mouth or the bacteria gain entrance to the circulation therefrom. Chronic rheumatoid arthritis, the etiology of which was heretofore completely in the dark, is now definitely ascribed to toxemic effects from mouth infections. The teeth, perhaps even more than the tonsil, act as means of entrance to the circulation for many bacteria. Many streptococci, particularly the streptococcus viridans, the pneumococcus, the non-pus-forming diplococcus of Connellan and King, as well as the endameba buccalis, are found in the mouth. It is not surprising, therefore, that pneumonia, abscess of the lung, pyemia, etc., are conditions that may be expected to follow on untreated mouth infections.

Moreover, the continued toxemia from oral sepsis affects the glands of internal secretion. Disturbances in balance of the whole endocrinous system may follow. These effects are most patent in the thyroid gland, where overstimulation by the toxins may produce symptoms of hyperthyroidism. Likewise, glycosuria, and even true diabetes mellitus, may follow as a result of the toxic irritation of the endocrinous system. High blood pressure and the resulting circulatory disturbances are caused by the same toxemic conditions, affecting directly, or indirectly through the glands of internal secretion, the vegetative nervous system controlling the vasomotor system.

The consistency with which medical military officers have been rejecting recruits seems to show that they realized the true significance of oral infections. The resistance of recruits suffering with oral infection is low, and their susceptibility to disease and hardship very high.

It must be remembered that the mouth can represent almost the greatest amount of broken tissue surface through which bacteria may gain entrance to the body. A thorough mouth cleaning is perhaps a much more rational means of beginning the treatment of disease than even the much overdone intestinal cleaning-out. There is a very tangible danger in the treatment of oral sepsis, and that is in the use of strong antiseptics, which corrode or devitalize healthy tissue, or in the laceration of tissue by careless instrumentation. However, the lymphatic glands of the neck catch and stop much of the infection from the mouth and lessen what would otherwise be a tendency to much more systemic effects of oral sepsis.

MEDICAL NOTES.

Chicago City Council Ordinance for Control of Venereal Diseases.—The ordinance relating to the control of venereal diseases which was passed by the City Council of Chicago, June 29, 1917, reads as follows:

The ordinance,—

(*a*) declares syphilis, gonorrhea and chancroid to be contagious, infectious, communicable and dangerous to the public health;

(*b*) requires physicians, managers of hospitals and dispensaries, and all other persons who give treatment for venereal diseases, to mail, within three days of the first visit of the patient, to the department of health, a card stating the age, sex, color, marital condition, and occupation of the diseased person, nature and previous duration of the disease, and the probable origin;

(*c*) requires physicians to hand to patients afflicted with venereal disease, at the first examination, a circular of information and advice furnished by the department of health and also a copy of this ordinance;

(*d*) requires the physician to ascertain from the patient whether a physician has been consulted heretofore and, if so, immediately to inform the physician or person who previously treated the patient. Should the physician, or person previously consulted, fail to receive such notice within ten days after the last appearance of such venereally diseased person, it shall be the duty of such physician to report to the health department the name and address of the patient;

(*e*) requires the commissioner of health to institute such measures for the protection of others against venereally diseased persons as he is already empowered to use to prevent the spread of other contagious, infectious or communicable diseases;

(*f*) provides that all reports shall be confidential and inaccessible to the public;

(*g*) holds parents of minors, having venereal disease and living with their parents, responsible for the compliance of such minors with the requirements of the ordinance;

(*h*) imposes a fine of not less than $25 nor more than $100 for each offense, on persons who violate, neglect or refuse to comply with these provisions.

London Death Rates in September.—Statistics recently published show that the total death rate of London in September, 1917, was only eleven per thousand inhabitants living. Among the several districts and boroughs the lowest rate was 6.6 in Woolwich, a southern suburb, and the highest was 14.9 in Bermondsey, a populous southern slum.

Lobar Pneumonia.—According to the experience of a life insurance company which has made a study of its mortality record for the past six years, lobar pneumonia causes more deaths than any of the other acute infectious diseases.

Although prevalent at the early ages, lobar pneumonia is not essentially a disease of early childhood. When it does occur in young children it is very frequently fatal. The disease reaps its greatest harvest at the ages over 65. At these ages it is one of the chief causes of death. The insurance figures, furthermore, show that the colored people have a much higher mortality rate than is found for the whites. This is true for both sexes and for every period of age. Pneumonia has a higher death rate for the male sex than for the female.

The Metabolic Unit.—Volunteering and the draft reduced the numbers of those associated with Dr. N. B. Potter at the Metabolic Unit recently established at the City Hospital, New York, so that it has been temporarily closed. Dr. Potter has transferred the work to Santa Barbara, California, where he is spending the winter, having made arrangements for its continuance at the Cottage Hospital. This Metabolic Unit is undertaking the study and treatment of gout, Bright's disease and diabetes, and the expenses are defrayed by contributions from a number of his patients and friends, as well as by a generous addition from the Carnegie Foundation.

Birth and Death Rates in Belgium.—The following report of the birth and death rates in Belgium appears in the London *Lancet:*

The death rate in Belgium has greatly increased in the last two years, and there has been a large decrease in the birth rate. While the number of births in the Brussels district in 1913 was 6417 (17 per 1000 of the population), and

the death rate 13.7, in the first six months of 1915 the birth rate was 14.3 and the death rate 14 per 1000. In the corresponding period of 1917 there were 3311 births (8.5 per 1000), and the death rate had risen to 19.3.

VALUABLE STATISTICAL STUDY MADE POSSIBLE BY THE WAR.—The following extracts from the statement of Dr. J. A. Murray, director of the Imperial Cancer Research Fund, in the Fifteenth Annual Report of the Fund, 1916-1917, will be of interest to those engaged in the study of cancer statistics:

"The importance which has always been attached by statisticians to the age-constitution of populations in which cancer mortality has to be studied, receives striking justification by the results recorded in the 78th Report of the Registrar-General (1915), published this year. The withdrawal of a large number of young men from civil life constitutes a most valuable statistical experiment, showing the effects of a sudden alteration in the age-constitution of a population. . . . The majority of the men withdrawn from civil life are under 35 years of age, and the cancer mortality figures for 1915 show the effects on a population of retaining the female sex in its normal proportions, while profoundly altering the relative proportions of the males above and below the age at which cancer is an important cause of death. . . The change in the male population is, on a large scale, affecting the whole country, and has taken place abruptly. It is analogous to those minor differences in age-constitution which have been attained slowly in isolated communities, and which go far to account for the phenomena of cancer villages and cancer streets. . . It is obvious that the varying conditions in limited areas at the present time must produce anomalies, and in fact, in some districts the deaths of males from cancer equal, or even exceed, those of females. Without the data necessary to effect the corrections for age and sex, crude death rates for such limited areas can only be misleading and may cause unnecessary alarm and distress.

"Undue importance should not be attached to the interruption in 1915 of the steady yearly increase of cancer mortality, the first since 1907. The conditions are abnormal, and as was pointed out in the Annual Report two years ago, the dislocation and diminution of the civil medical service by war conditions, may well affect the fidelity with which the national mortality figures reflect the absolute incidence of such a disease as cancer."

WAR NOTES.

RESERVE SUPPLY OF PHYSICIANS.—The Mayor's Committee on National Defense of New York has, through its committee on hospital and medical facilities, obtained figures showing the number of first-year students enrolled in a majority of the medical colleges of the country this year. The bearing of these figures on the continued supply of medical graduates in the event of a war of long duration are worthy of consideration. Among the seventy-six schools which recorded their figures there was an average increase in enrollment over the previous year of 16%. Among individual schools, those showing an increase of registration included the University of California with 35%, and Columbia University College of Physicians and Surgeons with 42%. Both Yale Medical School and Harvard Medical School show a decrease, the former 22% and the latter 11%. Washington University Medical School also shows a decrease of 22%. Johns Hopkins University Medical Department is about the same as in previous years.

ORTHOPEDIC WORK IN ENGLAND.—The following notice regarding the work of Major Joel E. Goldthwait, has appeared in *The British Medical Journal:*

"Major Joel E. Goldthwait, M.R.C., U.S.A., has returned to Europe, bringing with him from the United States forty-two medical officers, who will be distributed through the British orthopedic centers and later drawn for American orthopedic hospitals in France. They will receive training in British hospitals while serving under the American officers who were members of the first orthopedic unit brought over by Major Goldthwait in June last. When, after this training, they are drawn to the American service another group will be sent from the United States to take their place, and so on in successive groups. In this way a large number of positions will be filled for the work under the British director of military orthopedics by well-trained surgical assistants. The training of these younger men will fall upon the American orthopedic surgeons, while at the same time they will help to supply Sir Robert Jones with a large staff to meet the expansion of the orthopedic service. In addition Major Goldthwait is accompanied by three officers commissioned in the American Sanitary Corps, who will be employed in the establishment and development of the American curative workshops."

POSTHUMOUS HONOR TO MEDICAL STUDENT.—Second Lieutenant H. F. Parsons, of Bristol, England, who died of wounds received in battle, was awarded posthumously the V.C. for most conspicuous bravery. At the commencement of the war he was studying medicine in Bristol University.

RETURN OF SERBIAN COMMISSION.—The commission appointed by the American Red Cross to study methods of relief in Serbia will return to this country about Dec. 1. Dr. Frederick T. Lord and Dr. Eugene A. Crockett of Boston were members of the unit.

Death of Dr. G. P. Howe.—In a recent issue of the Journal was printed an account of the death of Dr. G. P. Howe, killed in action in France. The daily press has recently printed the following letter giving further details:

"British Red Cross.
18 Carlton House Terrace, S.W.I.
Capt. G. P. Howe, 10th Royal Fusiliers, fr. R. C. M. C.,

Dear sir: We beg to forward you our first report, which we have just received, with regard to the above officer.

Our informant, Sergt. W. Booth, 10th R. Fusiliers, returning to England on leave, gives us this information:

'This was in the rear of Polygon Wood. We were stopping a counter-attack. Capt. G. P. Howe was killed by shell. He was wounded slightly before, but he carried on. I saw the body after and helped to bury him. There was a military funeral, the American flag was used, and he was buried at Godezonne Farm with a cross on the grave.' "

New Medical Appointments for French Service.—The following appointments have been made by Surgeon-General Gorgas:

Director-general of surgery, Maj. John M. T. Finney, formerly of Johns Hopkins Hospital; director of laboratory, Lt.-Col. Joseph F. Silver; director of skin and venereal surgery, Maj. Hugh H. Young, formerly of Johns Hopkins.

Majs. Finney and Young volunteered their services to the government and were given commissions in the reserve corps of the medical department.

Tuberculosis in Army Camps.—It is stated that a small percentage of men in training in the army camps have showed tuberculosis symptoms, about four hundred in all. Every soldier who shows the slightest indication of having been infected by this disease is immediately discharged from the camp, and his name and address are reported to the health authorities of his home state.

War Relief Funds.—On November 24 the totals of the principal New England war relief funds reached the following amounts:

French Wounded Fund	$299,966.00
Surgical Dressings Fund	139,146.26
War Dogs' Fund	2,008.25

BOSTON AND MASSACHUSETTS.

Week's Death Rate in Boston.—During the week ending Nov. 24, 1917, the number of deaths reported was 216, against 263 last year, with a rate of 14.58, against 18.04 last year. There were 33 deaths under one year of age, against 37 last year.

The number of cases of principal reportable diseases were: diphtheria, 107; scarlet fever, 36; measles, 55; whooping cough, 46; typhoid fever, 3; tuberculosis, 62.

Included in the above were the following cases of non-residents: diphtheria, 25; scarlet fever, 3; typhoid fever, 1; tuberculosis, 6.

Total deaths from these diseases were: diphtheria, 8; measles, 1; whooping cough, 2; tuberculosis, 21.

Included in the above were the following non-residents: diphtheria, 1; tuberculosis, 4.

Hospital Bequest.—By the will of the late Mrs. Evelyn O. Weston of Boston, the Children's Hospital receives a gift of $5000 and the Convalescent Home of the Children's Hospital receives a share of a trust fund.

New Salem Hospital.—The new hospital at Salem, Mass., was opened for inspection on Nov. 17, and will soon be ready to admit patients. The hospital will accommodate 150 patients. It consists of a group of buildings made up of the main building, an operating building, domestic building, heating plant, and a coal pocket with a capacity of eight hundred tons, and plans have been drawn and the site set aside for a nurses' home.

The main building faces the south, and terraces and open balconies are connected with the various wards. On the first floor it has rooms for the trustees, offices and library, and other conveniences for the administration department; the west wing has the men's surgical ward and the east wing the women's surgical ward, while directly above these are the medical wards and two isolation wards for contagious cases. On the third floor are the maternity ward and private rooms for patients. On the fourth floor will be the nurses' rooms. The operating building is connected with the main building by a passage; the domestic department is connected with the main building by a passage and has a kitchen with the latest devices, including a refrigerating plant.

Boston Tuberculosis Association.—The annual meeting of the Boston Association for the Relief and Control of Tuberculosis was held at 3 Joy Street, on Nov. 22. Besides the routine business there were addresses, as follows: Dr. John F. O'Brien, chairman board of trustees, Boston Consumptives' Hospital, "The Development of the Boston Consumptives' Hospital from the Standpoint of the Trustees"; Dr. Edwin A. Locke, chief of visiting medical staff of Boston Consumptives' Hospital, "Work of Boston Consumptives' Hospital Proper"; Dr.

Cleaveland Floyd, director of out-patient clinic, Boston Consumptives' Hospital, "Review of Eleven Years' Work of the Out-Patient Department of the Boston Consumptives' Hospital"; Mrs. Anna M. Staebler, secretary of committee on health in industry, "Preventive Value of Industrial Nursing."

Obituary.

WILLIAM CALDWELL STEVENS, M.D.

WILLIAM CALDWELL STEVENS, M.D., died in Worcester, October 17, 1917, after an acute illness of one day only, aged 62.

He was born in Barre, Mass., December 16, 1854, the son of Charles Emery and Caroline E. Caldwell Stevens. His father was for many years registrar of probate for Worcester County, and in the family residence at 24 Boynton Street Dr. Stevens had his legal home from his majority to his decease—nearly a half century.

Young Stevens was graduated from the Worcester High School in 1872, and in that year entered Amherst, from which college he received his degree in 1876.

Following an early bent of mind, he spent the ensuing year in The Normal Art School of Boston. The next year he taught the High School of Dudley, and the two years subsequent at Cushing Academy in Ashburnham. Entering Harvard Medical School in 1879, he was graduated therefrom in 1882.

He served an interneship in the Rhode Island Hospital, and subsequently, as ship-surgeon, voyaging to Madeira. He then served as *locum tenens* in Ashfield, in which town he was so well liked that he was formally asked to settle there, but his sense of honor and medical etiquette forbade his accepting the invitation, and he opened an office on Pearl Street, and later on Pleasant Street, Worcester, where he paid special attention to diseases of the nose and throat.

He became secretary of the Worcester District Medical Society in 1887 and served a three-year term.

Failing health led him to give up his office for a time and he gradually drifted to the pursuit of art as a painter of landscapes, for which profession he had long had a strong desire and in which he finished his career.

Among the many notable artists Worcester has given the world in the last two generations, Dr. Stevens was, in the opinion of competent critics, one of the best. He knew colors, and all of his studies possess brilliant charm in quality of tone and draftsmanship. The rolling hills and fertile valleys of Worcester County were his inspiration. A perspective, showing a background of slate-blue mountains, with blue sky overhead, seemed to enthuse him most of all. He went to his great out-doors in any weather, and so the landscape of this vicinity has found an interpretation at his hand in every mood of the seasons' turning.

The joy he felt as he settled into his sketching-stool and fixed his easel beside the freshet-brooks of spring, in the birch thickets and oak groves of summer, or among the snow-clad hills of the drear and melancholy days of fall and winter, are all revealed in these sure and rapid transcripts; and in them he has been able, as Tolstoi has said "to pass his emotion to the others."

GEORGE O. WARD, M.D.,
For Worcester District Medical Society.

Miscellany.

WAR WORK OF AMERICAN MEDICAL WOMEN.*

BY ELIZA M. MOSHER, BROOKLYN, N. Y.

THE second annual meeting of the Medical Women's National Association, Dr. Bertha Van Hoosen of Chicago, President, was held in New York City, June, 1917. In view of the pressing need of physicians and surgeons in the war zone and in the devastated districts of Europe, a War Service Committee was appointed by the Association to deal with the situation. This body created an Executive Committee, with defined powers, of which Dr. Rosalie Slaughter Morton was unanimously elected chairman. Dr. Morton's selection for this post was a wise one. The Serbian government had bestowed upon her a decoration for her service in that country. In France special privileges had been given her to inspect and study the French hospitals, and after returning home from foreign duty she has still kept in close touch with the work.

Mr. Leo Schlesinger, of New York City, placed at the disposal of the committee a suite of rooms in his office building, 637 Madison Avenue, admirably suited to its purpose, and there, early in June, the committee was installed and intensive work began. Before the committee had completed its organization, Dr. Franklin Martin, chairman of the General Medical Board of Washington, asking for an outline of its plan of work. This outline, which Dr. Morton presented in person, received the unanimous approval of the board, and Dr. Morton was appointed a member of it and chairman of a committee of nine women physicians from different parts of the country, who were selected from a list of twelve submitted to Dr. Martin.

This committee of women physicians of the

*A résumé of the first quarterly report of the Chairman of the Women's Hospital Committee to the Medical Women's National Association.

General Medical Board may be regarded in the light of a congressional committee, its constituency being the women physicians of the United States. If the latter wish to have force and efficiency, organization is necessary. This committee of nine members is not permitted to increase the membership of the General Medical Board; obviously, therefore, it could not encompass the extensive work now going forward under the American Women's Hospitals, which, it is hoped, the general coöperation of women throughout the country will make even more extensive and thorough, and consequently of more value to the general board. We are now in a position to supply the data necessary to supplement that on the cards sent out from Washington, and on file there.

Copies of the outline prepared for the General Medical Board were laid before Col. J. R. Kean, director of the Department of Military Relief of the American Red Cross and the Surgeon-General of the Army, General Gorgas. They both expressed the greatest interest in and approval of the work. General Gorgas said that if the war continued for any length of time, the services of every woman doctor in the country would doubtless eventually be needed.

To anticipate this need, the plan of work, with registration blanks, was mailed to 5000 medical women, asking them to enroll. On October 6, at the time the first quarterly report of the American Women's Hospitals was issued, 115 women had registered as follows:

I, Women's units, 150; II, women's units to Allies' armies, 110; III, service in established units, 103; IV, maternity units to devastated regions, 84; V, village practice, 25; VI, for service in any of the above five, without choice, 110. The registration blanks are still coming in, and it is hoped that every woman physician in the country will record herself as being willing to serve her country in its hour of need.

In September the Red Cross asked for two units of women doctors to go immediately to Roumania. Their departure has been delayed for diplomatic reasons, incident to the situation in Russia. There are also in readiness forty doctors, who may be called within the next thirty days, and units have been arranged which can be mobilized within a few hours.

The American Women's Hospitals' flag and proper insignia, designed by Miss Brenda Putnam, a niece of that brilliant pioneer among women physicians, the late Mary Putnam Jacobi, has been adopted. The flag is blue and white; the drooping wings, the symbols of the American Women's Hospitals, are grouped around a shield bearing the name "American Women's Hospitals." The pins of bronze are sheltering wings, denoting protection and comfort, with the emblem of the various branches of the service placed upon them.

Open meetings of the American Women's Hospitals were held every Thursday afternoon throughout the past summer, and will be continued indefinitely. These meetings, presided over by Dr. Morton, or in her absence by Dr. Emily Dunning Barringer, the vice-chairman, have been of great interest, not only to the members of the organization, but to the general public.

Inspiring speeches by friends of the organization, and officers, doctors and nurses returned from the front have been a feature of these meetings. One of the most interesting of these was the address made by M. Liebert, the French Consul-General at New York.

An important branch of the American Women's Hospitals is that of the A. V. A. (American Volunteer Aid). This body was formed after the British V. A. D. (Volunteer Aid Department), and is in a thriving condition. Those wishing to join are given forms on which must be entered all data concerning non-medical women who wish to be laboratory assistants, ambulance drivers, stretcher-bearers, interpreters, dietitians, clerks, etc. A number will be needed in the units already in readiness. These lay assistants have a distinctive uniform for both identification and protection.

The Surgeon-General of the army has expressed his willingness to place in base hospitals, as contract-surgeons, women physicians as anesthetists, radiographers, and laboratory workers at a salary to be arranged by contract, and not to exceed $1800 per year. The need for laboratory workers is so great that the American Women's Hospitals have opened courses in this branch at the Women's Medical College of Pennsylvania; Women's Hospital, New York; and at the Research Laboratories of the New York City Board of Health. In them courses will be given to college women who have already studied chemistry and biology, in order to fit them, at a nominal expense, to become laboratory technicians, and to assist our physicians.

Any physician connected with laboratories which offer such courses in the different parts of the United States, and women wishing to apply for this training are requested to take up the matter immediately with the National Chairman of Laboratory Work, Dr. Martha Wollstein, No. 1, West 81st Street, New York City.

The Chairman of the Committee on Army Hospitals in the home zone, both for acute and convalescent cases, is Dr. Mary Almira Smith, 33 Newbury Street, Boston, Mass. The American Women's Hospitals have in Boston, two hospitals in readiness for convalescent cases and several others near New York. Its Women's Army General Hospital of New York, which has recorded its personnel and equipment in the War Department at Washington, has been told by Surgeon-General Gorgas that it will be notified when this is needed, and that it has the same status as all other army hospitals in the home zone.

The Women's Committee of the General Medical Board has two meetings, July 29 and September 29. A registration card was sent to the women physicians of the United States, with a view to ascertaining how many would be willing to serve in base hospitals as contract-surgeons, radiographers, laboratory workers and dressers of wounds. These cards are now being filed in Washington for reference in case need arises to place women in base hospitals, to release men for field hospital service.

The following are the regulations regarding contract practice:

1. Contract-surgeons do not receive pensions, except by special act of Congress.

2. The Government pays for transportation, quarters, heat and light, the same as furnished the first lieutenants.

3. There is no additional pay for foreign service; the contract specifies where the service is to be, and the amount to be received for this special service.

4. $1800 a year is the maximum, the minimum being whatever agreed to for the particular service to be rendered.

5. The amount is regulated by agreement; the surgeon states his price and the Government accepts or rejects; or *vice versa*.

6. The immediate superiors are the commissioned officers, of whatever rank in command at the station where the contract-surgeon serves, even although they be only first lieutenants.

The Surgeon-General's office expressed an interest in knowing how many women wished to become members of the Army Reserve Corps, and a letter was sent by the General Medical Board Committee of Women Physicians to the presidents of medical women's organizations, asking an expression of preference for this service, but comparatively few made their offer of war service absolutely contingent upon their becoming *officers* in the Army Reserve Corps.

It is the intention of the Medical Women's National Association to continue the work of this War Service Committee until the end of the war, if the need for it continues to exist.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1917.

General Prevalence.—The 4292 cases of communicable diseases reported during October show a considerable increase over the September total of 3004 and the October, 1916, total of 3227 cases. This increase of 1065 cases over the October, 1916, total is confined chiefly to diphtheria and measles.

There were 1152 cases of diphtheria reported for the month, an increase of 557 cases over the corresponding month last year. This brings out the seriousness of the diphtheria situation, for the prevalence of the disease has been increasing since early summer in the greater part of the State.

Anthrax.—Eight cases of anthrax were reported during the month. Five persons contracted the infection from five separate lots of China cow hides, two from China or India goat skins, and in one case the source of infection is unknown.

Diphtheria Carrier.—During the month four cases of diphtheria occurred among the pupils of a single schoolroom "somewhere in Massachusetts." Culturing of the pupils in this room disclosed two positive cultures. One was from a pupil who had a very mild attack of the disease, and the other was from a pupil who had not been sick recently, but who had diphtheria in August, 1916. A virulence test and a counter-virulence test, using the diphtheria bacilli from the throat of the latter pupil, showed the organisms to be virulent. Thus a chronic diphtheria carrier was found who had the organisms in his throat fourteen months after having had the disease. The occurrence demonstrates once again the efficiency of conscientious culturing of the throats of school children.

Lobar Pneumonia.—There were 152 cases of this disease reported in October, a marked increase as compared with 80 cases reported in September. Of these 152 cases, 23 were reported from Boston, the remaining 129 cases having a state-wide distribution.

Poliomyelitis.—Eleven cases of poliomyelitis were reported from ten widely separated communities.

Typhoid Carrier.—During the month one typhoid carrier was located who was apparently responsible for five cases of typhoid fever this year, and undoubtedly was the source of infection for cases in previous years. The carrier denied ever having had typhoid fever and has worked for several years on a milk farm. This year the farm on which he worked supplied six families, and typhoid fever cases occurred in four of the families.

Diseases on the Premises of Milk Handlers.—During the month four cases of scarlet fever were reported on a farm, producing milk that is shipped to Boston. As it was impossible satisfactorily to isolate the case, this milk supply was shut off.

EPIDEMICS AND OUTBREAKS.

Diphtheria.—An outbreak of 16 cases was reported from Great Barrington. Investigation showed that practically all attended the school in the Housatonic section of the town.

In North Attleboro 5 cases of diphtheria were reported in September, and an epidemic of 33 cases followed in October, being chiefly confined to one school. This epidemic followed the release of a diphtheria case with only one negative culture. Culturing of the school disclosed three persons with positive throat cultures, one of

whom was a teacher. A nurse was employed to aid in the supervision of the cases and to give instructions in quarantine of the homes.

An outbreak of 30 cases of diphtheria occurred in Holyoke, and all but two were found to attend the same school. Cultures were taken from all of the pupils at the school and produced negative cultures for the first two days, but the third time cultures were taken, four healthy carriers were found, two each in two rooms, and in another building the fifth healthy carrier was found.

Amesbury and West Springfield also had school outbreaks of diphtheria, reporting 21 cases and 10 cases, respectively.

In Easthampton 12 cases were reported for the month of October. In one family the disease spread after the appearance of the initial case because the parents objected to the giving of immunizing doses of antitoxin to the children who were not ill. As a result, another case of the disease appeared in this home.

Dysentery.—There were three cases of dysentery reported in the Medfield State Hospital during October, making a total of 60 cases for September and October. Institutional dysentery offers an exceptional opportunity for the bacteriological study of this disease if specimens of feces can be obtained early in the course of the disease. There were 31 deaths in the 60 cases reported.

Measles.—In Mattapoisett an outbreak of 35 cases of measles occurred among school children, as a result of a child sick with the measles riding to and from school in the same bus as other children before the case was recognized.

Typhoid Fever.—An epidemic of typhoid fever that started in September at the Tewksbury State Infirmary, during which month 22 cases were reported, continued for the first few days of October, 38 more cases making their appearance. The source of infection was not definitely determined, but was without doubt an undetermined healthy or convalescent carrier in the infirmary itself.

RARE DISEASES.

Anterior Poliomyelitis was reported from Abington 1, Chelsea 1, Danvers 1, Fall River 1, Haverhill 1, Hopedale 1, Lowell 1, Springfield 2, Stoneham 1 and Wellesley 1.

Anthrax was reported from Camp Devens 1, Lynn 2, Winchester 1 and Woburn 4.

Cerebrospinal Meningitis was reported from Camp Devens 1, Boston 4, Cambridge 1, Chelsea 1, Fall River 1, Holyoke 1, Malden 1 and Worcester 1.

Dog-bite was reported from Auburn 1, Boston 2, Brockton 1, Holliston 2, Lawrence 1, Lowell 1, and Newburyport 1.

Dysentery was reported from Dartmouth 3, Greenfield 1, Lawrence 3, Medfield 3, New Bedford 1, and Salem 1.

Malaria was reported from Boston 3, Chelsea 1, Douglas 1, Marblehead 1, and Pittsfield 1.

Pellagra was reported from Boston 1, Lowell 1, Tewksbury 1, and Worcester 1.

Septic Sore Throat was reported from Amherst 1, Boston 1, Gloucester 1, Lexington 4 and Medford 1.

Tetanus was reported from Pittsfield 1.

Trachoma was reported from Boston 5, Cambridge 1, Fitchburg 1, and Worcester 1.

ANTHRAX IN MASSACHUSETTS FOR THE CURRENT YEAR.

ANTHRAX is becoming increasingly prevalent since the beginning of the present war, as will be seen by the following table:

1908	5 cases	1913	8 cases
1909	7 "	1914	8 "
1910	7 "	1915	11 "
1911	6 "	1916	31 "
1912	11 "	*1917	39 "

* Nine months.

This marked increase the past two years is a result of the difficulty in obtaining sufficient hides through the normal trade channels by the manufacturer to supply the increased demand.

As a result, hides are now secured from new areas in foreign lands, concerning which the knowledge of prevalence of diseases is meager.

For the first nine months of the present year 39 cases of anthrax have been reported, of which number 6 were fatal. There were 38 cases of external anthrax and one of pulmonary anthrax, this latter being a worker in a hide warehouse. Of the 39 cases, 35 received infection from hides, three from hair and one from wool.

Recently it has been reported by English investigators* that cases of anthrax have been found that had symptoms simulating cerebrospinal meningitis, anthrax not being diagnosed until lumbar puncture had been carried out and the bacillus anthracis demonstrated in the spinal fluid. Thus it would seem advisable to have spinal fluid examination for cases of cerebrospinal meningitis among leather workers.

Anthrax is one of the diseases where the accuracy of the diagnosis is questionable unless the bacillus anthracis is found, and bacteriological smears from the lesion have been urged in all cases of the disease reported, with the following results:

Total	39 cases
Smears taken in	33 "
Smears negative for bacillus anthracis	8 "
Smears positive for bacillus anthracis	25 "
Diagnosis made at autopsy	1 case
No laboratory examination	5 cases
	39 cases

* See local government board report by Dr. Francis J. H. Coutts, M.D.

Of the 8 cases in which the smear was negative for the bacillus anthracis, 4 were isolated cases, each being the only case in the locality and handling hides which were not connected with other cases of the disease. The 4 remaining cases occurred at the time when other cases among their fellow-workmen, confirmed by smear examination, were reported, and were undoubtedly cases of the disease (Cases 4, 17, 29 and 35).

Of the 6 cases in which no smears were taken, there were several group instances suggesting that the diagnosis was correct. One group of 5 cases was reported, all having handled the same lot of hides (Cases 10, 11, 12, 17 and 29). Cases 10, 11 and 12 had positive smears for anthrax bacilli; Case 17 was negative and no smear was taken for Case 29.

Case 6 was infected at the same time as Case 16. In the latter, the bacillus anthracis was found in a smear.

Cases 20, 22 and 24 were infected at the same time from the same lot of hides. No smears were taken in Cases 20 and 22, but Case 24 was fatal and anthrax bacilli were found in the smear from the lesion.

Thus we have 25 cases confirmed bacteriologically, 7 cases associated with cases confirmed by smear examination, and 1 determined as anthrax at autopsy by pathological examination, making a total of 33 cases, undoubtedly anthrax.

In several instances where the first case reported has been in a stevedore or longshoreman, the factories and health department at the point of destination have been warned of the probable lot of hides infected.

For prevention of infection, the U. S. Bureau of Animal Industry regulations states that hides be immersed for not less than 48 hours in a 1 to 1000 solution of bichloride of mercury, or immersion in a 10% salt solution containing not less than 2% hydrochloric acid, for 48 hours.

For hair disinfection, the U. S. Bureau of Animal Industry regulations state that when hair or wool is suspected to be infected with anthrax, "that all of such wool or hair will be disinfected or sterilized by proper exposure to a temperature of not less than 212° F., for at least 15 minutes prior to any transfer or reshipment."

For hair disinfection, a recent report of the Local Government Board (New Series No. 112) states "that for steam disinfection to be successful, the cases or bales should be opened, the bundles removed and most of the strings cut, unless the temperature inside the steam disinfecting apparatus is maintained at 230° F. for half an hour."

SOCIETY NOTICE.

NEW ENGLAND PEDIATRIC SOCIETY.—A meeting of the New England Pediatric Society will be held at the Boston Medical Library on December 14, 1917, at 8.15 P.M.

I. Report of Treasurer.
II. Report of Council.
III. The following papers will be read:

The Treatment of Eneuresis with a Report of 26 Consecutive Recoveries.
W. R. P. Emerson, M.D., Boston.

The Cause and Treatment of Acidosis in Children.
W. McK. Marriott, M.D., St. Louis, Mo.

The Work of the State Committee on Child Conservation..
Fritz B. Talbot, M.D., Boston.

IV. Election of Officers.

Light refreshments will be served after the meeting.

MAYNARD LADD, M.D., *President*,
RICHARD M. SMITH, M.D., *Secretary*.

RECENT DEATHS.

SIR DAVID CALDWELL MCVAIL, former professor of clinical medicine at St. Mungo's College, died in Glasgow on November 4, at the age of 72 years. He was well known as an authority on diseases of the respiratory organs and made many contributions to the literature of this subject.

WILLIAM GIBSON CRAIG, M.D., died at his home in Springfield, November 15, aged 49. He was a graduate of the Jefferson Medical College, Philadelphia, in 1892, and practised ophthalmology and otology. He was a Fellow of the Massachusetts Medical Society and the American Medical Association.

Correspondence.

ANOTHER UNUSUAL CASE.

Reno, Nevada.

Mr. Editor:—

In the January 11 issue of your JOURNAL, on page 75, I notice the report of "An Unusual Case." I recently had one which was almost parallel. The night of January 11, W. M. G., a "broncho buster" came to me for relief of urinary retention. He gave a history of no bowel motion reaching over three days and that he had not been able to urinate between 9 A. M. and 11.30 P. M., when he called on me. On trying to pass a soft catheter I found a very marked spasm of the cut-off muscle, it taking me not less than quarter of an hour to get into the bladder. At this time the urine amounted to almost a quart. At 6.30 the following morning he again came in for relief from retention. I had the same trouble in getting into the bladder. At this time I gave him hyoscyamine to be taken 1/1000 grain every hour. At 5.30 P. M., he reported back that he had been able to empty his bladder voluntarily twice during the day and that peristalsis seemed to be starting up. I then gave him a cathartic pill to be taken at bed time. The next morning he reported that he had had a bowel action shortly after leaving my office the night before and that he had been able to urinate twice.

This man had been bucked off a wild pony a few weeks before coming to see me and the animal had fallen on him. He was knocked out completely and remained so for several hours, but seemed to feel no subsequent ill effects thereafter, other than some general soreness. There arose in my mind that there might be some central nerve injury and that the bladder and bowel conditions were due thereto. However, as the hyoscyamine seemed to relieve the spasm completely, I am rather of the idea that the cause lay elsewhere. I am free to confess that I could find no real cause for the strong and continued spasm. Otherwise the patient was absolutely well in every respect—one of our robust Nevada cowboys.

I am giving you the report of this case as it seems so closely allied to that of Dr. Bowker.

Yours very sincerely,
GEORGE L. SERVASS, M.D.,
Editor, *Western Medical Times*.